

## Medical Policy



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### Title: Treatment of Hyperhidrosis

#### Professional

Original Effective Date: September 23, 2009  
Revision Date(s): January 26, 2010;  
March 31, 2014; December 13, 2016  
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<b>Populations</b>	<b>Interventions</b>	<b>Comparators</b>	<b>Outcomes</b>
Individuals: • With primary focal hyperhidrosis (ie, axillary, palmar, plantar, craniofacial)	Interventions of interest are: • Iontophoresis	Comparators of interest are: • Topical antiperspirant • Oral medication • Botulinum toxin	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With primary axillary hyperhidrosis	Interventions of interest are: • Botulinum toxin type A or B	Comparators of interest are: • Topical antiperspirant • Oral medication	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With primary palmar hyperhidrosis	Interventions of interest are: • Botulinum toxin type A	Comparators of interest are: • Topical antiperspirant • Oral medication	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With primary palmar hyperhidrosis	Interventions of interest are: • Botulinum toxin type B	Comparators of interest are: • Topical antiperspirant • Oral medication	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With primary plantar hyperhidrosis	Interventions of interest are: • Botulinum toxin type A or B	Comparators of interest are: • Topical antiperspirant • Oral medication	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With primary focal hyperhidrosis (ie, axillary, palmar, plantar, craniofacial)	Interventions of interest are: • Microwave treatment	Comparators of interest are: • Topical antiperspirant • Oral medication • Botulinum toxin	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With primary focal hyperhidrosis (ie, axillary, palmar, plantar, craniofacial)	Interventions of interest are: • Radiofrequency ablation	Comparators of interest are: • Topical antiperspirant • Oral medication • Botulinum toxin	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With primary axillary hyperhidrosis	Interventions of interest are: • Surgical excision of axillary sweat glands	Comparators of interest are: • Topical antiperspirant • Oral medication • Botulinum toxin	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With primary axillary and palmar hyperhidrosis	Interventions of interest are: • Endoscopic transthoracic sympathectomy	Comparators of interest are: • Topical antiperspirant • Oral medication • Botulinum toxin	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With primary plantar hyperhidrosis	Interventions of interest are: • Lumbar sympathectomy	Comparators of interest are: • Topical antiperspirant • Oral medication	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With severe secondary gustatory hyperhidrosis	Interventions of interest are: • Iontophoresis • Botulinum toxin	Comparators of interest are: • Diet • Topical medications	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With severe secondary gustatory hyperhidrosis	Interventions of interest are: • Tympanic neurectomy	Comparators of interest are: • Diet • Topical medications	Relevant outcomes include: • Symptoms • Quality of life • Treatment-related morbidity

## **DESCRIPTION**

Hyperhidrosis, or excessive sweating, can lead to impairments in psychological and social functioning. Various treatments for hyperhidrosis are available, such as topical antiperspirant agents (eg, aluminum chloride 20% solution), oral medications, botulinum toxin, and surgical procedures.

## **Background**

### **Hyperhidrosis**

Hyperhidrosis has been defined as excessive sweating, beyond a level required to maintain normal body temperature, in response to heat exposure or exercise. It can be classified as primary or secondary. Primary focal hyperhidrosis is idiopathic in nature, typically involving the hands (palmar), feet (plantar), or axillae (underarms). Secondary hyperhidrosis can result from a variety of drugs, (eg, tricyclic antidepressants, selective serotonin reuptake inhibitors, or underlying diseases/conditions, (eg, febrile diseases, diabetes mellitus, menopause). Secondary hyperhidrosis is usually generalized or craniofacial sweating.

Secondary gustatory hyperhidrosis is excessive sweating on ingesting highly spiced foods. This trigeminovascular reflex typically occurs symmetrically on scalp or face and predominately over forehead, lips, and nose. Secondary facial gustatory, occurs independently of the nature of the ingested food. This phenomenon frequently occurs after injury or surgery in the region of the parotid gland. Frey syndrome is an uncommon type of secondary gustatory hyperhidrosis that arises from injury to or surgery near the parotid gland resulting in damage to the secretory parasympathetic fibers of the facial nerve. After injury, these fibers regenerate, and miscommunication occurs between them and the severed postganglionic sympathetic fibers that supply the cutaneous sweat glands and blood vessels. The aberrant connection results in gustatory sweating and facial flushing with mastication. Aberrant secondary gustatory sweating follows up to 73% of surgical sympathectomies and is particularly common after bilateral procedures.

The consequences of hyperhidrosis are primarily psychosocial in nature. 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, which is a simple qualitative measure to identify specific sites of involvement.

### **Therapeutic Options**

A variety of therapies have been investigated for primary hyperhidrosis, including topical therapy with aluminum chloride, oral anticholinergic medications, iontophoresis, intradermal injections of botulinum toxin, endoscopic transthoracic sympathectomy, and surgical excision of axillary sweat glands. Treatment of secondary hyperhidrosis focuses on treatment of the underlying cause, such as discontinuing certain drugs or hormone replacement therapy as a treatment of menopausal symptoms.

Botulinum toxin is a potent neurotoxin that blocks cholinergic nerve terminals; symptoms of botulism include cessation of sweating. Therefore, intracutaneous injections have been investigated as a treatment of gustatory hyperhidrosis and focal primary hyperhidrosis, most frequently involving the axillae or palms. The drawback of this approach is the need for repeated injections, which have led some to consider surgical approaches.

Surgical treatment options include removal of the eccrine glands and/or interruption of the sympathetic nerves. 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. Surgical removal has been performed in patients with severe isolated axillary hyperhidrosis.

Various surgical techniques of sympathectomy may also be tried. The second (T2) and third (T3) thoracic ganglia are responsible for palmar hyperhidrosis, the fourth (T4) thoracic ganglion controls axillary hyperhidrosis, and the first (T1) thoracic ganglion controls craniofacial hyperhidrosis. Thoracic sympathectomy has been investigated as a potentially curative procedure, primarily for combined palmar and axillary hyperhidrosis unresponsive to nonsurgical treatments. While accepted as an effective treatment, sympathectomy is not without complications. In addition to the immediate surgical complications of pneumothorax or temporary Horner syndrome, compensatory sweating on the trunk generally occurs in most patients, with different degrees of severity. Medical researchers have investigated whether certain approaches (eg, T3 sympathectomy versus T4 sympathectomy) result in less compensatory sweating, but there remains a lack of consensus about which approach best minimizes the risk of this side effect. In addition, with lumbar sympathectomy for plantar hyperhidrosis, there has been concern about the risk of postoperative sexual dysfunction in both men and women.

Outcomes from different surgical and medical treatment modalities are best assessed by using a combination of tools. Quantitative tools include gravimetry, evaporimetry, and Minor starch iodine test. Qualitative assessment tools include general health surveys and hyperhidrosis-specific surveys. Of these, the Hyperhidrosis Disease Severity Scale (see Appendix Table 1) has had good correlation to other assessment tools and is practical in the clinical setting.

### **Regulatory Status**

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

In 2004 Botox® (botulinum toxin type A, Allergan Pharmaceuticals Ireland) was approved by FDA through the biologic license application (BLA) process for use to treat primary axillary hyperhidrosis (severe underarm sweating) that cannot be managed by topical

agents. In 2009, this product was renamed onabotulinumtoxinA. Other botulinum toxin products approved by FDA through the BLA process include:

- 2000: RimabotulinumtoxinB, marketed as Myobloc® (Solstice Neurosciences)
- 2009: AbobotulinumtoxinA, marketed as Dysport® (Medicis Pharmaceutical, Scottsdale, AZ)
- 2010: IncobotulinumtoxinA, marketed as Xeomin® (Merz Pharmaceuticals)

None of the other botulinum toxin products are specifically approved for treatment of hyperhidrosis.

On July 31, 2009, 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. 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 another 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 for marketing by FDA through the 510(k) process for treating primary axillary hyperhidrosis. This microwave device is designed to heat tissue at the dermal-hypodermal interface, the location of the sweat glands. Treatment consists of 2 sessions for a total duration of approximately 1 hour. Sessions occur in a physician's office and local anesthetic is used

**POLICY****A. Primary Focal Hyperhidrosis**

1. Treatment of primary focal hyperhidrosis using the following therapies (see Table PG1) may be considered **medically necessary** with any of the following medical complications:
  - a. acrocyanosis of the hands  
or
  - b. history of recurrent skin maceration with bacterial or fungal infections  
or
  - c. history of recurrent secondary infections  
or
  - d. history of persistent eczematous dermatitis despite medical treatments with topical dermatological or systemic anticholinergic agents

**Table PG1 Treatments Considered Medically Necessary**

<b>Focal Regions</b>	<b>Treatments Considered Medically Necessary</b>
<b>Axillary</b>	<ul style="list-style-type: none"> <li>▪ Aluminum chloride 20% solution</li> <li>▪ Botulinum toxin for severe primary axillary hyperhidrosis inadequately managed with topical agents, in patients <math>\geq 18</math> years</li> <li>▪ ETS (endoscopic transthoracic sympathectomy) and surgical excision of axillary sweat glands, if conservative treatment (ie, aluminum chloride or botulinum toxin, individually and in combination) has failed</li> </ul>
<b>Palmar</b>	<ul style="list-style-type: none"> <li>▪ Aluminum chloride 20% solution*</li> <li>▪ Botulinum toxin A products for severe primary palmar hyperhidrosis inadequately managed with topical agents, in patients <math>\geq 18</math> years</li> <li>▪ ETS, if conservative treatment (ie, aluminum chloride or botulinum toxin type A, individually and in combination) has failed</li> </ul>
<b>Plantar</b>	<ul style="list-style-type: none"> <li>▪ Aluminum chloride 20% solution</li> </ul>
<b>Craniofacial</b>	<ul style="list-style-type: none"> <li>▪ Aluminum chloride 20% solution</li> <li>▪ ETS, if conservative treatment (ie, aluminum chloride) has failed</li> </ul>

Aluminum chloride solution is approved by FDA for treatment of primary hyperhidrosis. At least 1 botulinum toxin product is FDA-approved for treatment in adults of severe axillary hyperhidrosis inadequately managed by topical agents.

ETS: endoscopic transthoracic sympathectomy; FDA: Food and Drug Administration.

2. Treatment of primary focal hyperhidrosis using the following therapies (see Table PG2) are considered **experimental / investigational**:

**Table PG2 Treatments Considered Experimental / Investigational**

<b>Focal Regions</b>	<b>Treatments Considered Experimental / Investigational</b>
<b>Axillary</b>	<ul style="list-style-type: none"> <li>▪ Axillary liposuction</li> <li>▪ Iontophoresis</li> <li>▪ Microwave treatment</li> </ul>
<b>Palmar</b>	<ul style="list-style-type: none"> <li>▪ RimabotulinumtoxinB</li> <li>▪ Iontophoresis</li> <li>▪ Microwave treatment</li> <li>▪ Radiofrequency ablation</li> </ul>
<b>Plantar</b>	<ul style="list-style-type: none"> <li>▪ Botulinum toxin</li> <li>▪ Iontophoresis</li> <li>▪ Lumbar sympathectomy</li> <li>▪ Microwave treatment</li> </ul>
<b>Craniofacial</b>	<ul style="list-style-type: none"> <li>▪ Botulinum toxin</li> <li>▪ Iontophoresis</li> <li>▪ Microwave treatment</li> </ul>

## B. Secondary Hyperhidrosis

### *Secondary Gustatory Hyperhidrosis*

1. The following treatments would be considered **medically necessary** for the treatment of severe secondary gustatory hyperhidrosis. A list of gustatory hyperhidrosis conditions are: Frey syndrome, encephalitis, syringomyelia, diabetic neuropathies, herpes zoster parotitis, parotid abscess)
  - a. aluminum chloride 20% solution
  - b. surgical options (ie, tympanic neurectomy), if conservative treatment has failed.
2. Other treatments are considered **experimental / investigational** as a treatment for severe secondary gustatory hyperhidrosis including, but not limited to:
  - a. botulinum toxin
  - b. iontophoresis
3. Treatment of hyperhidrosis is considered **not medically necessary** in the absence of functional impairment or medical complications.

### Policy Guidelines

1. Absent evidence to the contrary, botulinum toxin products are considered to have a class effect.
2. A multispecialty working group have defined primary focal hyperhidrosis as a condition characterized by visible, excessive sweating of at least 6 months in

duration without apparent cause and with at least 2 of the following features:

- a. bilateral and relatively symmetric sweating
  - b. impairment of daily activities
  - c. frequency of at least once per week
  - d. age at onset younger than 25 years
  - e. positive family history, and
  - f. cessation of focal sweating during sleep
3. The Hyperhidrosis Disease Severity Scale (HDSS) is used by patients to rate the severity of their symptoms on a scale of 1 to 4:

Score	Definition
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

## **RATIONALE**

This evidence review has been updated with searches of the MEDLINE database. Most recently, the literature was reviewed through March 22, 2016. Following is a summary of the key literature to date.

### **Treatment for Primary Focal Hyperhidrosis (ie, Axillary, Palmar, Plantar, Craniofacial) Iontophoresis**

The published literature on iontophoresis as a treatment of hyperhidrosis is sparse. A 2003 TEC Assessment on iontophoresis for a variety of medical conditions concluded that the evidence was insufficient to determine whether its impact on the treatment of any type of hyperhidrosis exceeded those of placebo or an alternative treatment.<sup>1</sup> TEC Assessment investigators identified only 3 small studies (range, N-18 patients), all of which were conducted in patients with palmar hyperhidrosis.

Several case series and 1 randomized controlled trial (RCT) have been identified since 2003. The RCT compared iontophoresis to an alternative intervention but did not provide data on the efficacy of this therapy compared with placebo.<sup>2</sup> In 2014, Rajagopal et al in India compared iontophoresis to botulinum toxin in patients with palmar hyperhidrosis. The trial included 60 patients with had a baseline Hyperhidrosis Disease Severity Scale (HDSS) score of 3 or 4 (see Appendix Table 1 for scoring).<sup>3</sup> Patients were randomized to treatment with iontophoresis 3 times weekly or to 1 botulinum toxin injection in each hand, with 2 weeks between treatments. HDSS scores were recorded at 4 weeks; nonresponders were permitted to crossover to the other treatment arm. At the end of the initial 4 weeks, improvement (defined as decrease of at least 1 point in HDSS score) was identified in 24 (80%) of 30 patients in the botulinum toxin group and 14 (47%) of 30 patients in the iontophoresis group (p=0.007). Sixteen patients in the iontophoresis arm crossed over to the botulinum toxin arm, with 12 showing excellent improvement after an additional 4 weeks. In contrast, only 1 of the 6 patients who crossed over to the iontophoresis arm showed improvement after a second 4-week treatment period. In this relatively small sample with a relatively short intervention period, iontophoresis was less effective than botulinum toxin.

Among the case series is a 2014 retrospective study from Turkey that included 21 pediatric patients under age 18.<sup>4</sup> Most patients (n=16) had palmoplantar hyperhidrosis. Nineteen patients completed the course of 21 tap water iontophoresis sessions. Among study completers, mean self-report treatment effectiveness score, rated on a 0-to-10 visual analog scale, was 6.36 at the end of treatment. Seventeen (89.5%) of 19 patients reported a 50% or more decrease in sweating at the end of treatment. Another representative series is a 2013 study from Ireland that included 28 patients.<sup>5</sup> Patients received a minimum of 9 treatments over 21 days in a clinical setting. Twenty (80%) of the 25 patients for whom data were available after hospital administration of tap water iontophoresis reported a moderate or great amount of improvement in symptoms and a moderate or great improvement in quality of life,

### ***Section Summary: Iontophoresis***

There is insufficient evidence that iontophoresis is an effective treatment of primary focal hyperhidrosis. The single RCT found iontophoresis less effective than botulinum toxin in the short-term treatment of palmar hyperhidrosis. RCTs are needed to show that iontophoresis is more effective than placebo treatment and/or appropriately designed trials that demonstrate iontophoresis is at least as effective as alternative therapies.

### **Botulinum Toxins**

Several RCTs address botulinum toxin injections for treatment of axillary and palmar hyperhidrosis.<sup>6-10</sup> The discussion will be grouped by region and toxin type as dictated by trial.

#### ***Primary Axillary Hyperhidrosis Treated With Botulinum Toxin Type A or B***

One of the larger RCTs was published in 2007.<sup>6</sup> This trial was an industry-sponsored, multicenter, double-blind, placebo-controlled efficacy and safety study of botulinum toxin type A in patients with persistent bilateral primary axillary hyperhidrosis. Enrollment criteria included a resting sweat production of at least 50 mg/axilla in 5 minutes and an HDSS score of 3 or 4 (see Appendix Table 1). A total of 322 patients were randomized to botulinum toxin type A (onabotulinumtoxinA) 50 U or 75 U or placebo. Retreatment after 4 weeks was allowed in patients with at least 50 mg of sweat (per axilla) over 5 minutes and an HDSS score of 3 or 4. Following the first injection, 75% of patients in the botulinum toxin type A groups showed at least a 2-point improvement in HDSS score, compared with 25% of patients in the placebo group. Sweat production decreased by 87% (75 U), 82% (50 U), and 33% (placebo). (Similar results were obtained in patients requiring a second treatment.) Median duration of effect was 197 (75 U), 205 (50 U), and 96 days (placebo). Seventy-eight percent (n=252) of patients completed the 52-week trial: 96 (87%) of 110 in the 75-U group, 83 (80%) of 104 in the 50-U group, and 73 (68%) of 108 in the control group. Intention-to-treat analysis at 52 weeks showed more than 2-point improvement on HDSS score in 54 (49%) patients 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 approximately 10% of all groups, with a mean pain duration of 2.4 days (10-day maximum).

In 2005 Baumann et al reported on a placebo-controlled RCT evaluating use of botulinum toxin type B for axillary hyperhidrosis. Like another Baumann trial (reported below), this RCT did not address whether patients had failed previous treatments for hyperhidrosis. The axillary hyperhidrosis trial included 20 patients who received subcutaneous injections of rimabotulinumtoxinB 2500 U or 0.5 mL per axilla (n=15) or placebo (n=5).<sup>8</sup> Patients who received placebo were offered botulinum toxin type B, at subsequent injections. Data were available on efficacy for the 18 patients (15 in the initial botulinum toxin B group and 3

crossovers). There was a statistically significant improvement in axillary hyperhidrosis from baseline (before receiving an active injection) to day 30, according to patient and physician assessment. Details on efficacy outcomes were not reported. Mean length of time to return to baseline sweating levels in these 18 patients was 151 days (range, 66-243 days). Sixteen patients reported 61 adverse events during the study. Five (8%) of 61 adverse events were determined to be trial related: 4 axillary bruising events and 1 instance of injection-site pain. Eleven (18%) adverse events were determined to be probably related to the trial: dry eyes (n=3), dry mouth (n=5), and indigestion (n=3). Flu-like symptoms were reported by 6 (30%) of 20 patients; however, the trial period coincided with flu season. In 2010, Dresser et al published an RCT including 46 patients with bilateral axillary hyperhidrosis and a previously stable onabotulinumtoxinA treatment for at least 2 years.<sup>11</sup> Patients received onabotulinumtoxinA 50 U in 1 randomly selected axilla and incobotulinumtoxinA 50 MU in the other axilla. All patients completed the study. According to patient self-report in structured interviews, there were no between-group differences in therapeutic effect, including onset latency, extent, and duration, and no differences in injection-site pain. Moreover, clinical examination did not identify any differences between the 2 sides in the diffuse sweating pattern.

A small, double-blind RCT published in 2007 by Talarico-Filho et al included 20 patients with primary axillary hyperhidrosis who had sweat production greater than 50 mg/minute.<sup>12</sup> Patients received injections of 2 types of botulinum toxin A: onabotulinumtoxinA 50 U in 1 axilla and abobotulinumtoxinA 150 U in the other. Outcomes did not differ significantly between groups (eg, sweat rate was reduced by a mean of 98% in the onabotulinumtoxinA group and 99% in the abobotulinumtoxinA group;  $p>0.05$ ).

A few RCTs have compared botulinum toxin types A and B in patients with primary axillary hyperhidrosis. In 2011, Frasson et al conducted a small randomized trial of axillary hyperhidrosis treated with botulinum toxin type A and type B.<sup>13</sup> This trial included 10 patients with idiopathic focal axillary hyperhidrosis unresponsive to other nonsurgical treatments. Patients received onabotulinumtoxinA 50U in 1 axilla and rimabotulinumtoxinB 2500 U in the contralateral axilla. Gravimetry was performed at baseline and follow-up as an objective measure sweat production. At each follow-up point, the decrease in sweat weight from baseline was significantly greater on the type B side than on the type A side. For example, after 1 month, the sweat weight in 5 minutes was 13% of the baseline value on the type A side and 4% of the baseline value on the type B side ( $p=0.049$ ). By 6 months, the sweat weight returned to 91% of baseline on the type A side and to 56% of baseline weight on the type B side ( $p=0.02$ ). Findings were similar for sweating area. All patients tolerated injections of types A and B well, and none reported systemic adverse effects. This trial did use a higher dosage of botulinum toxin type B than previous studies.

A 2015 RCT by An et al randomly assigned 24 patients with symmetrical axillary hyperhidrosis to receive injections of onabotulinumtoxinA 50 U in 1 axilla and rimabotulinumtoxinB 1500 U in the other (ie, a conversion rate of 1:30 was used).<sup>14</sup> Baseline HDSS scores were 2 (n=9), 3 (n=14), and 4 (n=1); those who scored 3 or 4 were categorized as having severe axillary hyperhidrosis. The primary efficacy outcome (the proportion of patients with an HDSS score of 1 or 2 at the 2-week follow-up) was 100% in each group ( $p=1.00$ ). At 12 weeks, all patients still had a score of 1 or 2 on the HDSS ( $p=1.00$ ) and at 20 weeks, 80% in each group had an HDSS score of 1 or 2 ( $p=1.00$ ). A decrease of 2 points or more from baseline on the HDSS was reported at week 2 in 86.7% in each group ( $p=1.00$ ); at week 12, the same decrease was reported in 80.0% in the

botulinum toxin type A group and 86.7% in the botulinum toxin type B group ( $p=0.64$ ); and at week 20, the same decrease was only reported in 13.3% of the botulinum toxin type A group and in 6.7% of the botulinum toxin type B group ( $p=0.56$ ). No major systemic adverse effects were reported in any patients.

### ***Primary Palmar Hyperhidrosis Treated With Botulinum Toxin Type A***

Two double-blind randomized trials compared onabotulinumtoxinA and incobotulinumtoxinA. In 2014, Campanati et al included 25 patients with moderate-to-severe primary palmar hyperhidrosis resistant to aluminum chloride or iontophoresis.<sup>15</sup> Patients received injections of incobotulinumtoxinA in a randomly selected hand and onabotulinumtoxinA in the other hand. Botulinum toxin was given at a fixed dosage per square centimeter of the hand. There were no statistically significant differences in outcomes between groups. This included changes in HDSS score and the extent of sweating assessed using the Minor test.

### ***Primary Palmar Hyperhidrosis Treated With Botulinum Toxin Type B***

In another 2005 placebo-controlled, randomized, Baumann et al evaluated botulinum toxin type B for palmar hyperhidrosis. Like the previous Baumann trial, this RCT did not discuss whether patients had failed previous treatments for hyperhidrosis. This RCT included 20 patients with excessive palmar sweating.<sup>7</sup> Fifteen patients received injections of rimabotulinumtoxinB, 50,000 U per palm and 5 received placebo. Nonresponders were offered an injection of botulinum toxin type B at day 30. At day 30, the 2 quality-of-life measures were significantly better in the botulinum toxin group than in the control group. However, the difference was not statistically significant for efficacy in physician analysis of the palmar iodine starch test at day 30 ( $p=0.56$ ). No further details were provided on the efficacy outcome measures. Mean duration of action according to self-report in 17 patients (15 in the initial treatment group, 2 who crossed over from the placebo group) was 3.8 months (range, 2.3-4.9 months). Patients were asked about specific adverse events: 18 (90%) of 20 reported dry mouth/throat, 12 (60%) reported indigestion, 12 (60%) reported excessively dry hands, 12 (60%) reported muscle weakness, and 10 (50%) reported decreased grip strength.

### ***Primary Plantar Hyperhidrosis Treated With Botulinum Toxin Type A or B***

There is a lack of RCTs on use of any botulinum toxin formulation for plantar hyperhidrosis.

### ***Section Summary: Botulinum Toxins***

Evidence from RCTs supports the efficacy and safety of botulinum toxin for treating axillary hyperhidrosis. In addition, RCTs have found similar outcomes among botulinum type A formulations and between botulinum type A and B. For palmar hyperhidrosis, evidence from RCTs supports the efficacy and safety of botulinum toxin type A for treating palmar hyperhidrosis but 1 small RCT did not clearly demonstrate efficacy of botulinum toxin type B. There is a lack of RCTs on use of any botulinum toxin formulation for plantar hyperhidrosis.

### **Microwave Treatment**

A 2012 RCT evaluated a microwave device for treating primary focal hyperhidrosis.<sup>16</sup> This device applies microwave energy to superficial skin structures with the intent of inducing thermolysis of the eccrine and apocrine sweat glands. This industry-sponsored, double-blind trial randomized 120 adults with primary axillary hyperhidrosis 2:1 to active ( $n=81$ ) or sham ( $n=39$ ) treatment. Treatment consisted of 2 sessions, separated by approximately 2 weeks. Patients who responded adequately after 1 session or declined further treatment did not undergo the second session; a

third procedure was allowed within 30 days for patients who still had a high level of sweating after 2 sessions. All patients in the sham group had 2 sessions. In the active treatment group, 11 (9%) patients had 1 session, 60 (74%) had 2 sessions, and 10 (8%) patients had 3 sessions. The primary efficacy end point was an HDSS score of 1 or 2 (see Appendix Table 1) at the 30-day follow-up; HDSS score at 6 months was a secondary outcome. A total of 101 (84%) of 120 patients completed the study. At 30 days, 89% of the active treatment group and 54% of the sham group had an HDSS score of 1 or 2 ( $p < 0.001$ ). At 6 months, 67% of the active treatment group versus 44% of the sham group had an HDSS score of 1 or 2 ( $p = 0.02$ ). Unblinding occurred at 6 months. Twelve-month data were available for the active treatment group only; 69% reported an HDSS score of 1 or 2. There were 45 procedure-related adverse events in 23 (28%) of the active treatment group versus 5 (13%) of the sham group. The most frequently reported adverse event was altered sensation; no serious adverse events were reported. Compensatory sweating was reported by 2 patients in each group (mean duration, 52 days). The authors noted that study data provided an opportunity to identify areas for improvement in the treatment protocol including waiting longer between treatments and using a higher dose of energy at the second session.

A 2012 industry-sponsored case series reported on 31 patients with primary axillary hyperhidrosis treated with microwave therapy using the miraDry system.<sup>17</sup> All patients had an HDSS score of 3 or 4 at baseline. The primary efficacy outcome (the proportion of patients whose HDSS score decreased to 1 or 2) was 28 (90%) at 6 and 12 months posttreatment. Longer term skin-related adverse effects (that all resolved over time) were altered sensation in the skin of the axillae (65% of patients; median duration, 37 days) and palpable bumps under the skin of the axillae (71% of patients; median duration, 41 days).

### ***Section Summary: Microwave Treatment***

One RCT and case series provide insufficient evidence that microwave treatment improves the health outcome for primary focal hyperhidrosis. The RCT reported short-term benefit of microwave treatment in reducing hyperhidrosis, but also reported a high rate of skin-related adverse effects (eg, pain, altered sensation). Additional controlled trials with long-term follow-up in the treatment and control groups, a longer period of blinding, and a consistent treatment protocol are needed to confirm the efficacy of this treatment and to better define the risk-benefit ratio.

### **Radiofrequency Ablation**

A 2013 study evaluated radiofrequency ablation (RFA) as a treatment for patients with severe bilateral palmar hyperhidrosis resistant to conservative treatment.<sup>18</sup> The study was conducted in Turkey and retrospectively reviewed outcomes after RFA ( $n = 48$ ) or transthoracic sympathectomy ( $n = 46$ ). Patients were not randomized to treatment group. After a mean follow-up of 15 months, palmar hydrosis was absent in 36 (75%) patients in the RFA group versus 44 (96%) patients in the surgery group. The difference in outcomes between groups was statistically significant, favoring the surgical intervention ( $p < 0.01$ ). Six patients in each group reported moderate or severe compensatory sweating ( $p = 0.78$ ).

### ***Section Summary: Radiofrequency Ablation***

One nonrandomized comparative study represents insufficient evidence for RFA as a treatment of hyperhidrosis. In this single available study, RFA was inferior to surgical sympathectomy.

## Surgical Interventions

### *Surgical Excision of Axillary Sweat Glands*

Surgery may involve removal of the subcutaneous axillary 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.<sup>19</sup> Depending on the completeness of surgical excision, treatment is effective in 50% to 95% of patients.

### *Endoscopic Transthoracic Sympathectomy*

Several RCTs and 1 meta-analysis have compared different surgical approaches; there were no sham-controlled RCTs. In 2011, Deng et al published a meta-analysis of data from RCTs and observational studies published to 2010 that evaluated endoscopic thoracoscopic sympathectomy for patients with palmar hyperhidrosis.<sup>20</sup> The authors pooled outcome data from different approaches to sympathectomy (ie, single-ganglia blockage [T2, T3, T4], multiganglia blockage [T2-3, T2-4, T3-4]). (Note that T refers to rib.) Based on these analyses, the reviewers concluded that T3 (11 studies) and T3-4 (2 studies) had the “best” clinical efficacy (ie, postoperative resolution of symptoms). The T3 approach resulted in a 97.9% pooled efficacy rate, and the T3-4 approach resulted in a 100% pooled efficacy rate. In the studies for which data were available, the pooled rate of postoperative compensatory sweating was 40% after T3 surgery. Data on compensatory sweating after T3-4 surgery were available from only 1 study (60 patients); a pooled analysis could not be performed.

Subsequent RCTs have compared levels of sympathectomy. These trials tended to have relatively small sample sizes (ie, <100 patients). For example, a 2011 study by Baumgartner et al in the United States included 121 patients with disabling palmoplantar hyperhidrosis.<sup>21</sup> Patients were randomized to receive bilateral sympathectomy over T2 (n=61 patients) or T3 (n=60 patients). Six (5%) of 121 patients (3 in each group) were considered treatment failures (ie, had recurrent palmar sweating to a bothersome level). There were no significant differences between groups in the reported subjective change in plantar or axillary sweating after surgery. At 6 months, the mean (SD) level of compensatory sweating (0-10 severity scale) was 4.7 (2.7) for the T2 group and 3.8 (2.8) for the T3 group (p=NS). Similarly, at 1 year, the mean (SD) severity rating of compensatory sweating was 4.7 (2.5) in the T2 group and 3.7 (2.8) in the T3 group (p=0.09). A 2013 trial by Yuncu et al in Turkey included 60 patients with axillary hyperhidrosis; 17 were assigned to T3-4 surgery and 43 to T3 surgery.<sup>22</sup> There were no significant differences between groups in postoperative satisfaction. At 1-year follow-up, the incidence of compensatory sweating was lower in the T3 group (79%) than in the T3-4 group (100%).

There also are case series on transthoracic sympathectomy for treating primary focal hyperhidrosis.<sup>23-26</sup> Case series have generally reported high success rates for palmar and axillary hyperhidrosis, although there are potential adverse effects, most commonly compensatory sweating. For example, in 2014, Karamustafouglu et al in Turkey reported on 80 patients with primary hyperhidrosis (axillary and/or palmar).<sup>24</sup> All 80 patients responded to a questionnaire a mean of 35 months after surgery. Seventy-one (89%) of the 80 patients were very satisfied with the surgical outcome, and the other 11% were dissatisfied. Compensatory sweating was reported by 62 (78%) patients. Moreover, a 2013 series reported on complications after thoracic sympathectomy in 1731 patients with palmar, axillary, or craniofacial hyperhidrosis.<sup>23</sup> Thirty days after surgery, 1531 (88%) of patients reported compensatory sweating. Among the 1531 patients, compensatory sweating was mild in 473 (31%), moderate in 642 (42%), and severe in 416 (27%). Gustatory sweating was reported by 334 (19%) of the 1731 patients.

### ***Lumbar Sympathectomy***

No RCTs on the use of lumbar sympathectomy to treat primary plantar hyperhidrosis were identified, but several case series were identified. A 2009 series by Rieger et al from Austria evaluated surgical results in 90 patients (59 men, 31 women with severe plantar hyperhidrosis).<sup>27</sup> Thirty-seven (41%) patients had only plantar hyperhidrosis and 53 (59%) had plantar and palmar hyperhidrosis. All patients had previously used other treatments including topical antiperspirant (ie aluminum chloride). There were a total of 178 procedures, 90 on the right side and 88 on the left side. The technique involved resecting a segment of the sympathetic trunk between the third and fourth lumbar bodies together with the ganglia (L3 and/or L4). After a mean follow-up of 24 months (range, 3-45 months), hyperhidrosis was eliminated in 87 (97%) of 90 patients. Postoperative neuralgia occurred in 38 (42%) patients between the seventh and eighth day. The pain lasted less than 4 weeks in 11 patients, 1 to 3 months in 19 patients, 4 to 12 months in 5 patients, and more than 12 months in 3 patients. Three men reported temporary sexual symptoms; 1 was incapable of ejaculation for 2 months. None of the women reported postoperative sexual dysfunction.

In 2010, Reisfeld reported on a study of bilateral endoscopic lumbar sympathectomy in 63 patients with focal plantar hyperhidrosis from a specialized hyperhidrosis clinic in the United States.<sup>28</sup> Thirteen (21%) patients were male and 50 (79%) were female. A clamping method was used in which clamps were placed at L3 (47%), L4 (52%), and L2 (1%). There was a learning curve with this procedure, and 5 early cases were converted to an open procedure. Fifty-six (89%) patients had previously undergone some form of thoracic sympathectomy, and all had tried conservative measures. After a mean follow-up of 7 months, all patients considered their plantar hyperhidrosis symptoms to be "cured" or "improved"; 97% reported "cure." All patients with previous thoracic sympathectomy had some degree of compensatory sweating. After lumbar sympathectomy, 51 (91%) of the 56 patients reported that their compensatory sweating was unchanged. In the 7 patients who did not have a previous thoracic sympathectomy, 1 reported mild and 6 reported moderate compensatory sweating. Male patients reported no sexual problems; investigators did not report possible sexual problems among female patients.

It is worth noting that, in contrast to earlier concerns about this procedure being associated with risks of permanent sexual dysfunction in men and women, these case series found no instances of permanent sexual dysfunction. A 2004 review from a multispecialty working group on hyperhidrosis stated that lumbar sympathectomy is not recommended for plantar hyperhidrosis because of associated sexual dysfunction; this article did not cite any data documenting sexual dysfunction.<sup>29</sup> To date, there are very few studies on endoscopic lumbar sympathectomy for focal plantar hyperhidrosis and no comparative studies.

### ***Section Summary: Surgical Interventions***

Sweat gland excision has been found to be effective in 50% to 95% of appropriately selected patients.

RCTs and a meta-analysis of RCTs support the efficacy of endoscopic transthoracic sympathectomy at various levels for palmar and axillary hyperhidrosis. These data are complemented by case series, which have found high efficacy rates, but also high rates of compensatory sweating for these conditions.

There is insufficient evidence in support of lumbar sympathectomy for treating plantar hyperhidrosis; case series have found lower rates of efficacy for plantar compared to axillary or palmar hyperhidrosis, and there are concerns for adverse effects in sexual functioning. There are insufficient data to conclude that any particular approach to surgery results in lower rates of compensatory sweating.

### **Treatment for Severe Secondary Gustatory Hyperhidrosis**

#### **Iontophoresis**

As noted in the section on primary focal hyperhidrosis, a 2003 TEC Assessment on iontophoresis for a variety of medical conditions concluded that the evidence was insufficient to determine whether iontophoresis for the treatment of any type of hyperhidrosis improves outcomes.<sup>1</sup> Neither the TEC Assessment nor subsequent literature searches have identified any RCTs evaluating iontophoresis for gustatory hyperhidrosis.

#### **Botulinum Toxin**

A 2015 Cochrane review did not identify any RCTs or quasi-randomized RCTs evaluating the efficacy of botulinum toxin injections for the treatment of gustatory hyperhidrosis as a result of Frey syndrome.<sup>30</sup> No RCTs were identified in literature searches.

#### **Tympanic Neurectomy**

Review articles by Clayman et al (2006)<sup>31</sup> and de Bree et al (2007)<sup>32</sup> have described various medical and surgical treatments for Frey syndrome. Tympanic neurectomy is described as a treatment for Frey syndrome, with satisfactory control reported in 82% of patients. In addition, this surgical treatment is generally definitive without a need for repeated interventions.

### **Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.

**Table 1. Summary of Key Trials**

<b>NCT No.</b>	<b>Trial Name</b>	<b>Planned Enrollment</b>	<b>Completion Date</b>
<b>Ongoing</b>			
NCT01930604	Botulinum Toxin Treatment in Craniofacial, Inguinal, Palmar, Plantar and Truncal Hyperhidrosis	274	Oct 2017

NCT: national clinical trial.

### **Summary of Evidence**

For individuals who have primary focal hyperhidrosis (ie, axillary, palmar, plantar, craniofacial) who receive iontophoresis, the evidence includes 1 randomized controlled trial (RCT) and case series. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. The RCT found that iontophoresis was less effective than botulinum toxin in the short-term treatment of palmar hyperhidrosis. Additional RCTs are needed comparing iontophoresis to sham or active treatment in patients with various types of primary focal hyperhidrosis. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have primary axillary hyperhidrosis who receive botulinum toxin type A or B, the evidence includes RCTs. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. Placebo-controlled RCTs have generally found better outcomes in the botulinum toxin groups. Several RCTs have compared botulinum toxin type A formulations in

patients with primary axillary hyperhidrosis and have compared botulinum toxin type A and B formulations in patients with axillary hyperhidrosis. Although these studies had small sample sizes, their findings suggest that, with appropriate dosage adjustments, there are similar levels of efficacy and adverse events. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have primary palmar hyperhidrosis who receive botulinum toxin type A, the evidence includes RCTs. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. Placebo-controlled RCTs have generally found better outcomes in the botulinum toxin groups. RCTs comparing botulinum toxin type A formulations in patients with primary palmar hyperhidrosis have generally found no significant difference in outcomes. Although these studies had small sample sizes, their findings suggest that, with appropriate dosage adjustments, there are similar levels of efficacy and adverse events. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have primary palmar hyperhidrosis who receive botulinum toxin type B, the evidence includes 1 RCT. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. One small placebo-controlled RCT did not clearly demonstrate the efficacy of botulinum toxin type B in patients with palmar hyperhidrosis. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have primary plantar hyperhidrosis who receive botulinum toxin type A or B, the evidence includes no RCTs. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. RCTs are needed comparing botulinum toxin to placebo or active treatment in patients with primary plantar hyperhidrosis. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have primary focal hyperhidrosis (ie, axillary, palmar, plantar, craniofacial) who receive microwave treatment, the evidence includes 1 RCT and case series. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. The RCT, conducted in patients with primary axillary hyperhidrosis, found short-term benefit of microwave treatment versus sham therapy, but there was a high rate of skin-related adverse effects. Additional RCTs are needed comparing radiofrequency ablation to sham or active treatment in patients with various types of primary focal hyperhidrosis. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have primary focal hyperhidrosis (ie, axillary, palmar, plantar, craniofacial) who receive radiofrequency ablation, the evidence includes a nonrandomized cohort study. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. The cohort study, conducted in patients with palmar hyperhidrosis, found a higher cure rate in the surgery group than in the radiofrequency ablation group, and found a similar rate of compensatory sweating in both groups. RCTs are needed comparing radiofrequency ablation to sham or active treatment in patients with various types of primary focal hyperhidrosis. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have primary axillary hyperhidrosis who receive surgical excision of axillary sweat glands, the evidence includes review articles. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. This treatment is considered standard of care for this

indication. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have primary axillary and palmar hyperhidrosis who receive endoscopic transthoracic sympathectomy, the evidence includes several RCTs, a meta-analysis, and case series. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. The meta-analysis found a high rate of clinical efficacy after endoscopic transthoracic sympathectomy, although the rate of postoperative compensatory sweating was substantial; other studies had similar findings. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have primary plantar hyperhidrosis who receive lumbar sympathectomy, the evidence includes case series. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. Case series have reported high rates of clinical efficacy, but findings are inconclusive due to lack of control groups. Moreover, there have been substantial rates of compensatory sweating and concerns about adverse effects on sexual functioning. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have severe secondary gustatory hyperhidrosis who receive iontophoresis or botulinum toxin, the evidence includes uncontrolled studies and systematic reviews. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. The systematic reviews did not identify any relevant RCTs; RCTs are needed to evaluate the safety and efficacy of these conditions for treatment of severe secondary gustatory hyperhidrosis. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have severe secondary gustatory hyperhidrosis who receive tympanic neurectomy, the evidence includes uncontrolled studies and systematic reviews. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. This treatment is considered standard of care for this indication, and has high success rates, without need for repeated interventions. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

## Practice Guidelines and Position Statements

### Society of Thoracic Surgeons

In 2011, a task force of the Society of Thoracic Surgeons published an expert consensus statement on the surgical treatment of hyperhidrosis.<sup>33</sup> The document states that endoscopic thoracic sympathectomy is the treatment of choice for patients with primary hyperhidrosis. It further recommended the following treatment strategies (with R referring to rib and the number to which rib):

- R3 interruption for palmar hyperhidrosis; an R4 interruption is also reasonable. The authors note a slightly higher rate of compensatory sweating with R3, but R3 is also more effective at treating hyperhidrosis.
- R4 or R5 interruption for palmar-axillary, palmar-axillary-plantar or axillary hyperhidrosis alone; R5 interruption is also an option for axillary hyperhidrosis alone.
- R3 interruption for craniofacial hyperhidrosis without blushing; an R2 and R3 procedure is an option but may lead to a higher rate of compensatory sweating, and also increases the risk of Horner syndrome.

### American Academy of Neurology

In 2008, the American Academy of Neurology created guidelines for use of botulinum toxin for the treatment of autonomic disorders and pain.<sup>34</sup> These guidelines included the following recommendations for botulinum toxin injection as a treatment of hyperhidrosis:

“...should be offered as a treatment option for ... axillary hyperhidrosis ... (Level A), should be considered for palmar hyperhidrosis and drooling ... (Level B), and may be considered for gustatory sweating ... (Level C).”

### National Institute for Health and Care Excellence

The U.K.'s National Institute for Health and Care Excellence issued guidance in 2014 stating that there is sufficient evidence for the efficacy and safety of endoscopic thoracic sympathectomy for primary facial blushing to support the use of the procedure.<sup>35</sup>

### U.S. Preventive Services Task Force Recommendations

Not applicable.

### **CODING**

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

#### CPT/HCPCS

32664	Thoracoscopy, surgical; with thoracic sympathectomy
64650	Chemodenervation of eccrine glands; both axillae
64653	Chemodenervation of eccrine glands; other area(s) (eg, scalp, face, neck), per day
69676	Tympanic neurectomy
J0585	Injection, onabotulinumtoxinA, 1 unit
J0586	Injection, abobotulinumtoxinA, 5 units
J0587	Injection, rimabotulinumtoxinB, 100 units
J0588	Injection, incobotulinumtoxinA, 1 unit

- A variety of iontophoretic devices can be purchased for use in the home. There are no specific HCPCS codes for these pieces of DME [durable medical equipment]. Code E1399 (Durable medical equipment, miscellaneous) might be used.
- Botulinum toxin may be coded for using HCPCS codes: J0585, J0586, J0587, J0588.

#### ICD-9 Diagnoses

705.21	Primary focal hyperhidrosis
705.22	Secondary focal hyperhidrosis
780.8	Generalized hyperhidrosis

#### ICD-10 Diagnoses (Effective October 1, 2015)

L74.510	Primary focal hyperhidrosis, axilla
L74.511	Primary focal hyperhidrosis, face
L74.512	Primary focal hyperhidrosis, palms

- L74.513 Primary focal hyperhidrosis, soles  
 L74.52 Secondary focal hyperhidrosis  
 R61 Generalized hyperhidrosis

## REVISIONS

09-23-2009	Policy added to the bcbsks.com web site as a stand-alone policy. Hyperhidrosis was previously discussed in the Botulinum Toxin medical policy.										
01-26-2010	<p>In Policy Section:</p> <ul style="list-style-type: none"> <li>▪ Clarified policy language by changing 4.A. From: "Botulinum toxin when other treatments have failed" to " Botulinum toxin when symptoms are at a severity level of 3 or 4 (see severity scale below) and other treatments have failed"</li> <li>▪ Clarified policy language by changing B.1. from: " Thoracic sympathectomy when symptoms are severe and other treatments have failed" to "Thoracic sympathectomy when symptoms are at a severity level of 3 or 4 (see severity scale below) and other treatments have failed"</li> </ul>										
03-31-2014	<p>Description section updated</p> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ Revised to create distinction between Primary Focal Hyperhidrosis and Secondary Hyperhidrosis.</li> <li>▪ Updated Primary Focal Hyperhidrosis information From:            "Treatment of hyperhidrosis resulting in significant impairment of daily activities may be considered medically necessary with the following:            A. Non-surgical: 1. Topical treatments such as aluminum chloride, glutaraldehyde, anticholinergics, 2. Systemic treatments, such as anti-cholinergics, tranquilizers, 3. Iontophoresis, 4. Botulinum toxin when symptoms are at a severity level of 3 or 4 (see severity scale below) and other treatments have failed            B. Surgical: 1. Thoracic sympathectomy when symptoms are at a severity level of 3 or 4 (see severity scale below) and other treatments have failed"            To:            "Treatment of primary hyperhidrosis may be considered medically necessary with any of the following medical complications:            1. acrocyanosis of the hands; or            2. history of recurrent skin maceration with bacterial or fungal infections; or            3. history of recurrent secondary infections; or            4. history of persistent eczematous dermatitis in spite of medical treatments with topical dermatological or systemic anticholinergic agents.</li> </ul> <table border="1"> <thead> <tr> <th>Focal Regions</th> <th>Treatments Considered Medically Necessary</th> <th>Treatments Considered Investigational</th> </tr> </thead> <tbody> <tr> <td><b>Axillary</b></td> <td> <ul style="list-style-type: none"> <li>▪ aluminum chloride 20% solution*</li> <li>▪ botulinum toxin* for severe primary axillary hyperhidrosis that is inadequately managed with topical agents*, in patients 18 years and older</li> <li>▪ 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</li> </ul> </td> <td> <ul style="list-style-type: none"> <li>▪ axillary liposuction</li> <li>▪ iontophoresis</li> <li>▪ microwave treatment</li> </ul> </td> </tr> <tr> <td><b>Palmar</b></td> <td> <ul style="list-style-type: none"> <li>▪ aluminum chloride 20% solution*</li> <li>▪ botulinum toxin A products for severe</li> </ul> </td> <td> <ul style="list-style-type: none"> <li>▪ RimabotulinumtoxinB</li> <li>▪ iontophoresis</li> </ul> </td> </tr> </tbody> </table>		Focal Regions	Treatments Considered Medically Necessary	Treatments Considered Investigational	<b>Axillary</b>	<ul style="list-style-type: none"> <li>▪ aluminum chloride 20% solution*</li> <li>▪ botulinum toxin* for severe primary axillary hyperhidrosis that is inadequately managed with topical agents*, in patients 18 years and older</li> <li>▪ 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</li> </ul>	<ul style="list-style-type: none"> <li>▪ axillary liposuction</li> <li>▪ iontophoresis</li> <li>▪ microwave treatment</li> </ul>	<b>Palmar</b>	<ul style="list-style-type: none"> <li>▪ aluminum chloride 20% solution*</li> <li>▪ botulinum toxin A products for severe</li> </ul>	<ul style="list-style-type: none"> <li>▪ RimabotulinumtoxinB</li> <li>▪ iontophoresis</li> </ul>
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	<b>Plantar</b>	<ul style="list-style-type: none"> <li>▪ aluminum chloride 20% solution*</li> </ul>	<ul style="list-style-type: none"> <li>▪ botulinum toxin</li> <li>▪ iontophoresis</li> <li>▪ lumbar sympathectomy</li> <li>▪ microwave treatment</li> </ul>
	<b>Craniofacial</b>	<ul style="list-style-type: none"> <li>▪ aluminum chloride 20% solution*</li> <li>▪ endoscopic transthoracic sympathectomy (ETS), if conservative treatment (i.e., aluminum chloride) has failed</li> </ul>	<ul style="list-style-type: none"> <li>▪ botulinum toxin</li> <li>▪ iontophoresis</li> <li>▪ microwave treatment</li> </ul>
	<p>▪ Added section on indications for treatment of Secondary Gustatory Hyperhidrosis: "1.The following treatments would be considered medically necessary for the treatment of severe gustatory hyperhidrosis:</p> <ol style="list-style-type: none"> <li>a. aluminum chloride 20% solution*</li> <li>b. surgical options (i.e., tympanic neurectomy), if conservative treatment has failed.</li> </ol> <p>2. The following treatments are considered experimental / investigational as a treatment for severe gustatory hyperhidrosis including, but not limited to:</p> <ol style="list-style-type: none"> <li>a. botulinum toxin is considered investigational for treatment of gustatory hyperhidrosis. (See Policy Guidelines for list of conditions)</li> <li>b. iontophoresis</li> </ol> <p>*FDA approved indication (in the case of botulinum toxin, FDA approved for at least one botulinum toxin product)</p> <p>3. Treatment of hyperhidrosis is considered not medically necessary in the absence of functional impairment or medical complications."</p> <ul style="list-style-type: none"> <li>▪ Removed "Lumbar sympathectomy, axillary liposuction or resection of axillary sweat glands are considered experimental / investigational."</li> <li>▪ Added Policy Guidelines leaving reference to the Severity Scale.</li> </ul>		
	Rationale section updated		
	<p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Added CPT and HCPCS codes: 69676, J0586, J0588</li> <li>▪ Revised nomenclature for HCPCS codes: J0585, J0587</li> <li>▪ Added ICD-10 Diagnosis Codes</li> </ul>		
	References updated		
12-13-2016	Description section updated		
	<p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Item A 1 added "focal" and "using the following therapies (see Table PG1)" and removed "(see definition of primary hyperhidrosis in Policy Guidelines)" to read "Treatment of primary focal hyperhidrosis using the following therapies (see Table PG1) may be considered medically necessary with any of the following medical complications:"</li> <li>▪ Updated Table PG1 ad renamed to "Treatments Considered Medically Necessary"</li> <li>▪ Updated Table PG1 footnotes</li> <li>▪ Created Item A 2 to separate the experimental / investigational treatments from the medically necessary treatments with "Treatment of primary focal hyperhidrosis using the following therapies (see Table PG2) are considered experimental /</li> </ul>		

<p>investigational:" No changes to the E/I treatment were made.</p> <ul style="list-style-type: none"> <li>▪ Created Table PG2 pulling experimental / investigational treatments from old PG1 Table labeling as "Table PG2 Treatments Considered Experimental / Investigational"</li> <li>▪ In Item B 1 added "secondary" and "(A list of gustatory hyperhidrosis conditions are: Frey syndrome, encephalitis, syringomyelia, diabetic neuropathies, herpes zoster parotitis, parotid abscess)"</li> <li>▪ In Item B 1 removed "*FDA approved indication. Note: In the case of botulinum toxin, FDA approved for at least one botulinum toxin product."</li> <li>▪ In Item B 2 added "Other" and "secondary" and removed "The following" to read, "Other treatments are considered experimental / investigational as a treatment for severe secondary gustatory hyperhidrosis including, but not limited to:"</li> <li>▪ In Item B 2 a removed "is considered investigational for treatment of gustatory hyperhidrosis" to read "botulinum toxin"</li> <li>▪ Updated Policy Guidelines</li> </ul>
Rationale section updated
<p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Added HCPCS Codes: J0585, J0587</li> <li>▪ Updated coding notations.</li> </ul>
References updated

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