Nerve Fiber Density Measurement

Policy # 00240
Original Effective Date: 10/14/2009
Current Effective Date: 09/19/2018

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.

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 skin biopsy with epidermal nerve fiber density measurement for the diagnosis of small-fiber neuropathy to be **eligible for coverage.**

Patient Selection Criteria
Coverage eligibility for skin biopsy with epidermal nerve fiber density measurement for the diagnosis of small-fiber neuropathy may be considered when ALL of the following criteria are met:

- Individual presents with symptoms of painful sensory neuropathy; AND
- There is no history of a disorder known to predispose to painful neuropathy (e.g., diabetic neuropathy, toxic neuropathy, HIV neuropathy, celiac neuropathy, inherited neuropathy); AND
- Physical examination shows no evidence of findings consistent with large-fiber neuropathy, such as reduced or absent muscle-stretch reflexes or reduced proprioception and vibration sensation; AND
- Electromyography and nerve-conduction studies are normal and show no evidence of large-fiber neuropathy.

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 skin biopsy with epidermal nerve fiber density measurement for all other conditions, including, but not limited to, the monitoring of disease progression or response to treatment, to be **investigational.***

The use of skin biopsy with epidermal nerve fiber density measurement for the diagnosis of small-fiber neuropathy when patient selection criteria are not met is considered to be **investigational.***

Based on review of available data, the Company considers measurement of sweat gland nerve fiber density to be **investigational.***

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Background/Overview

PERIPHERAL NEUROPATHY

Most patients with peripheral neuropathy exhibit evidence of large fiber involvement, characterized by numbness, tingling, loss of deep tendon reflexes, and abnormal electrophysiologic studies. In contrast, damage to small fibers is not detected by routine nerve conduction studies. Patients with small fiber neuropathy, involving myelinated A delta and unmyelinated C fibers, may complain of severe pain and exhibit diminished thermal and pain perception. The pain, which is frequently reported in the feet, is described as burning, prickling, stabbing, jabbing, or tight band-like pressure. If there is involvement of autonomic C fibers, symptoms such as coldness, discoloration, and hyper- or hypohidrosis may be present. Small fiber neuropathy occurs most often in patients with diabetic neuropathy but may also be found in patients with impaired glucose tolerance, severe hypertriglyceridemia, metabolic syndrome, HIV infection, and toxic neuropathy from antiretroviral drugs. For many patients, no specific etiology is identified.

Diagnosis

Small fiber neuropathy is diagnosed clinically but has traditionally been a diagnosis of exclusion based on clinical findings and the absence of large fiber involvement, as determined by electrophysiologic studies. The disparity between subjective complaints and objective signs increases the difficulty of diagnosis. Also, conditions other than nerve fiber damage, including venous insufficiency, spinal stenosis, myelopathy, and psychosomatic disturbances, may mimic small fiber neuropathy.

Treatment

There is no curative treatment for small fiber peripheral neuropathy. Medications may be provided for pain management, and for some etiologies, treatment of the underlying condition (eg, glucose control, intravenous immunoglobulin, or plasma exchange) may be given to reduce progression of the disease and its symptoms.

Skin biopsy is used to assess the density of epidermal (intraepidermal) and sweat gland (sudomotor) nerve fibers using antibodies to a marker found in peripheral nerves. A specific test to assess intraepidermal nerve fiber (IENF) density and sweat gland nerve fiber density using skin biopsy and immunostaining of the tissue have been developed that allow the identification and counting of intraepidermal and sudomotor nerve fibers. Assessment of nerve fiber density typically involves a 3-mm punch biopsy of skin from the calf (and sometimes foot or thigh). After sectioning by microtome, the tissue is immunostained with anti-protein-gene-product 9.5 (PGP 9.5) antibodies and examined with immunohistochemical or immunofluorescent methods. This technique has improved research and contributed greatly to the understanding of small fiber neuropathy. Skin biopsy with measurement of IENF density has also been investigated as an objective measure for the diagnosis of small fiber neuropathy. Sweat gland nerve fiber density can be assessed from the same tissue prepared for IENF density testing provided that the biopsy sample is of sufficient depth. Tissue samples may also be counterstained to identify the boundaries of the sweat glands better.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA). These tests are available under the auspices of CLIA. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the FDA has chosen not to require any regulatory review of this test.

Assessment of IENF and SGNF density with *PGP 9.5* is commercially available with a biopsy kit, although IENF-density measurement (i.e., tissue preparation, immunostaining with *PGP 9.5*, and counting) may also be done by local research pathology labs. Some laboratories who offer IENF density testing include Therapath, Advanced Laboratory Services, Mayo Medical Laboratories, Corinthian Reference Lab, and Bako Integrated Physician Solutions.

Centers for Medicare and Medicaid Services (CMS)
There is no national coverage decision specifically on IENF density testing. The 2002 national coverage decision for services provided for the diagnosis and treatment of diabetic sensory neuropathy with loss of protective sensation (also known as diabetic peripheral neuropathy) (70.2.1) provided the following information:

> "… Medicare covers, as a physician service, an evaluation (examination and treatment) of the feet no more often than every six months for individuals with a documented diagnosis of diabetic sensory neuropathy and loss of protective sensation, as long as the beneficiary has not seen a foot care specialist for some other reason in the interim. Loss of protective sensation shall be diagnosed through sensory testing with the 5.07 monofilament using established guidelines, such as those developed by the National Institute of Diabetes and Digestive and Kidney Diseases guidelines. Five sites should be tested on the plantar surface of each foot, according to the National Institute of Diabetes and Digestive and Kidney Diseases guidelines. The areas must be tested randomly since the loss of protective sensation may be patchy in distribution, and the patient may get clues if the test is done rhythmically. Heavily callused areas should be avoided. As suggested by the American Podiatric Medicine Association, an absence of sensation at two or more sites out of 5 tested on either foot when tested with the 5.07 Semmes-Weinstein monofilament must be present and documented to diagnose peripheral neuropathy with loss of protective sensation."

Rationale/Source

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

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The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose.

NERVE FIBER DENSITY MEASUREMENT

Clinical Context and Test Purpose
The purpose of intraepidermal small fiber (IENF) density or sweat gland nerve fiber (SGNF) density measurement testing of patients who have a suspected idiopathic small fiber neuropathy or who have an established diagnosis or who are at risk of small fiber neuropathy is to provide objective information which may help to confirm the diagnosis of small fiber neuropathy.

The question addressed in this evidence review is: Does use of IENF or SGNF density measurement testing confirm the diagnosis of small fiber neuropathy leading to a change in management expected to improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant populations of interest are individuals with suspected idiopathic small fiber neuropathy or an established diagnosis of small fiber neuropathy or a suspected small fiber neuropathy.

Interventions
The relevant interventions of interest are IENF density measurement or a repeated IENF measurement or an SGNF density measurement.

Comparators
The relevant comparators of interest are standard clinical workup or continued medical monitoring.

Outcomes
The general outcomes of interest are test accuracy, change in disease status, reduction in symptoms such as pain, and quality of life.

Timing
Any associated effect on health outcomes resulting from testing and management changes may occur over a period of weeks to months.

Setting
Patients with small fiber neuropathy would be seen in the outpatient setting by a neurologist.

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Intraepidermal Nerve Fiber Density Measurement

Technically Reliable
A 2005 systematic review from the European Federation of Neurological Societies determined that skin biopsy from the distal leg or foot with immunostaining with anti-protein-gene-product 9.5 (PGP 9.5) is a safe, validated, and reliable technique for the determination of IENF density, indicating adequate technical performance of this test. European Federation Neurological Societies also concluded that IENF density is diagnostically efficient at distinguishing polyneuropathy patients (including small fiber neuropathy) from normal controls.

In 2010, Lauria et al published a multicenter study (8 sites) of normative reference values for IENF density at the distal leg. Groups that previously reported normative IENF density values using bright-field immunohistochemistry provided data to a coordinating center. Density data from 550 healthy subjects (age range, 18-84 years) in the United States, Europe, and Asia were included in the analysis. There was a significant decrease in IENF density in both men and women with age. For women, the 5th percentile ranged from 8.4 fibers per millimeter at 20 to 29 years of age to 1.6 fibers per millimeter at 80 years or older. For men, the 5th percentile ranged from 6.1 fibers per millimeter at 20 to 29 years of age to 1.7 at 80 years or older. IENF density was lower in men than in women between 20 and 69 years of age, but not for subjects 70 years or older. This finding might be limited by the smaller sample size in the older age groups. In addition, the analysis did not suggest that height, weight, or body mass index has a significant influence on IENF density normative scores (5th percentile).

Clinically Valid
Assessment of diagnostic accuracy necessitates that studies include a representative patient population with an appropriate spectrum of patients and that the test is compared with an independently assessed criterion standard. The European Federation Neurological Societies systematic review did not assess the more clinically relevant question, which is: What is the diagnostic accuracy of skin biopsy in distinguishing symptomatic patients with polyneuropathy from symptomatic patients without polyneuropathy? For example, in patients with painful feet, would skin biopsy accurately distinguish patients with polyneuropathy from other conditions causing painful feet?

To address these questions, the American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation performed a literature review (2009) to evaluate the diagnostic accuracy of IENF density in the detection of small fiber neuropathy. They adopted a clinical diagnosis of small fiber neuropathy as the independent reference standard for calculation of sensitivity and specificity. Eight studies were reviewed that employed a case-control design with patients with established polyneuropathy and normal controls. Significant differences were found between the 2 groups. For example, McArthur et al (1998) studied 98 normal controls and 20 patients who have sensory neuropathies. The density of epidermal nerve fibers in the controls was 13.8 per mm in the calf (5th percentile of controls, 3.8 per millimeter), with a significant mean

reduction in the study population (p value not reported) and a diagnostic efficiency of 88% (vs healthy controls). An earlier report (1997) by this group showed a mean IENF density of 4.9 per millimeter in 20 patients with sensory neuropathy and a mean IENF density of 16.3 per millimeter in 20 age-matched controls. However, none of the studies reviewed included an appropriate group of patients (ie, those with conditions causing lower-extremity pain or sensory complaints that might be confused with polyneuropathy). In addition, the sensitivity of IENF density ranged from 45% to 90% compared with healthy controls, indicating that the absence of reduced IENF density would not rule out polyneuropathy.

The American Association of Clinical Endocrinologists conducted an evidence review on diabetic neuropathy for its 2011 guidelines used to develop a comprehensive diabetes care plan. The evidence review found level 3 evidence (cross-sectional studies) that IENF density correlated inversely with cold and heat detection thresholds and is significantly reduced in symptomatic patients with normal findings from nerve conduction studies and those with metabolic syndrome, impaired glucose tolerance, and impaired fasting glucose, suggesting early damage to small nerve fibers. Level 3 evidence (surveillance studies) indicated that IENF density is reduced in painful neuropathy compared with that observed in painless neuropathy. Level 2 evidence (prospective cohort studies) indicated that diet and exercise interventions in impaired glucose tolerance lead to increased IENF density. Reviewers concluded these data suggested that IENF loss is an early feature of metabolic syndrome, prediabetes, and established diabetes and that the loss progresses with increasing neuropathic severity. Also, there may be nerve regeneration with treatment (diet and exercise).

The single prospective study (1999) identified in the 2009 American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine and American Academy of Physical Medicine and Rehabilitation literature review included a series of 117 patients presenting with painful bilateral l feet. In this report, a skin biopsy was done only in the subset of 32 patients who had normal nerve conduction studies, and the study did not compare the results of the IENF density with an independent reference standard to confirm the presence of small fiber neuropathy. American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation concluded that IENF density assessment is “possibly useful” to identify distal symmetric polyneuropathy, including small fiber neuropathy, in symptomatic patients with suspected polyneuropathy (level C recommendation). Future research recommendations included the need for studies to characterize the diagnostic accuracy of skin biopsy in distinguishing patients with suspected polyneuropathy (particularly small fiber neuropathy) from appropriate patients with sensory complaints or pain unrelated to peripheral neuropathy, using a predetermined reference standard.

The diagnostic accuracy of skin biopsy was assessed in a 2009 study of 210 patients who had signs of small fiber neuropathy from various conditions. The diagnosis of pure small fiber neuropathy (n=45) was established if patients had clinical symptoms and sensory deficits but preserved vibration and joint sense. Using the 5th percentile as a threshold (6.7 fibers per millimeter), the sensitivity of IENF density was 35%, and specificity was 95%.

Additional studies include large retrospective series. Devigili et al (2008) retrospectively reviewed 486 patients referred for suspected sensory neuropathy. This study lacked an independent reference standard, because the IENF results determined whether patients were included in the study group. Walk et al (2007) examined the concordance between foot IENF density and clinical findings in 106 patients with possible idiopathic small fiber neuropathy. An IENF density of 8 per millimeter was found to have the highest sensitivity (88%) and specificity (81%), using the sensory deficit to pinprick as the standard. In a 2009 review, Walk concluded that a reduction in IENF density provides supportive evidence of a loss of cutaneous efferents, but "clinical features remain paramount in the diagnostic process and the possibility of small fiber dysfunction is not excluded by an IENF density in the normal range."

Clinically Useful

An issue to consider for this diagnostic test is whether objective confirmation in patients with a clinical diagnosis of small fiber neuropathy will alter treatment decisions and lead to improved health outcomes. Oaklander et al (2013) prospectively evaluated whether small fiber neuropathy may have been the cause of symptoms in patients who had a prior diagnosis of fibromyalgia by an independent physician. Of 27 patients, skin biopsies were consistent with small fiber neuropathy (<5th percentile of the norm) in 41% compared with 3% of matched control subjects, leading to an investigation of other potential causes. A 2013 retrospective analysis by Boruchow and Gibbons found a change in diagnosis or management in 36 (52%) of 69 patients who had a skin biopsy at their institution for evaluation of possible small fiber neuropathy. Determination of low or borderline IENF density led to newly identified diseases in 8 patients, more aggressive diabetes management in 8 patients, and further laboratory testing in 4 patients. Of the 35 patients who had normal skin biopsies, 14 had new treatments and/or diagnoses, including musculoskeletal pain, plantar fasciitis, Morton neuroma, restless legs syndrome, lumbar spinal stenosis, Raynaud syndrome, peripheral nerve hyperexcitability, autoimmune autonomic ganglionopathy, and depression. The authors reported that examination findings were not effective at distinguishing patients with or without pathologic determination of small fiber neuropathy, and that some physicians at their institution appeared to use skin biopsies as a way to rule out, rather than rule in, a diagnosis of small fiber neuropathy. The authors did not report whether the changes in diagnosis or management led to improved health outcomes.

A 2011 review of the diagnosis and treatment of pain in small fiber neuropathy indicated that the history and physical exam are still considered the criterion standard and that further testing may be unnecessary, particularly in the context of an associated disease. However, authors suggested that IENF density measurement may provide diagnostic confirmation or additional guidance if the diagnosis is less clear. Thus, facilitating a diagnosis in patients with idiopathic small fiber neuropathy can lead to an end in the diagnostic odyssey and potentially change management.

Section Summary: Intraepidermal Nerve Fiber Density Measurement

The technical reliability of IENF staining with PGP 9.5 is adequate, reliably showing the density of small nerve fibers in the epidermal layer. IENF density decreases across age and sex in healthy controls and, therefore, density measurements in patients suspected of small fiber neuropathy are compared with age-

and sex-adjusted normative values. Few studies have prospectively compared the clinical validity of IENF density measurements in a population of patients suspected of small fiber neuropathy with an established reference standard. The available studies have shown low sensitivity and high specificity, suggesting that an IENF density below the 5th percentile of healthy controls may support a diagnosis of small fiber neuropathy, but IENF density above the 5th percentile cannot be used to rule it out.

There would be little benefit on health outcomes in patients who can be diagnosed clinically or who have a condition (eg, diabetes) associated with neuropathy. However, for individuals who have symptoms suggestive of neuropathy but no evidence of large nerve neuropathy and no disease associated with neuropathy (eg, diabetic neuropathy, toxic neuropathy, HIV neuropathy, celiac neuropathy, inherited neuropathy), establishing a cause for the symptoms is problematic. Thus, IENF density measurement may help diagnose idiopathic small fiber neuropathy, thereby ending the diagnostic odyssey and potentially changing management.

Repeated IENF Density Measurement
A number of trials are ongoing or have recently been completed that assess the efficacy of activity and medications on neuropathy (see Table 1). If successful, it might be determined that repeated IENF density measurements results in a change in management (eg, changing dose or class of medication). However, currently, no known treatments can alter the density of small nerve fibers in patients with symptomatic neuropathy. The clinical utility has not been demonstrated for monitoring changes in IENF density over time.

Sweat Gland Nerve Fiber Density Measurement

Technically Reliable
In a 2009 report, Gibbons et al evaluated SGNF density measurements in punch skin biopsies from 30 diabetic subjects and 64 controls; biopsies were sectioned and stained with PGP 9.5 and compared with confocal microscopy with stereology. Measurements of SGNF density were normalized by area due to the large variability in sweat gland size, and specific methods were used to reduce the high inter- and intrareviewer variability in manual outlining of sweat gland area. The authors noted nonspecific background staining of the sweat glands with PGP 9.5 that made it difficult to measure individual nerve fibers and sweat gland margins. There was an average of 1.6 sweat glands per biopsy. The blinded evaluation found a correlation (*r*) of 0.93 between SGNF density and the stereologic estimate of sweat gland nerve fiber length. The intrareviewer intraclass correlation coefficient was 0.886, and the interreviewer intraclass correlation coefficient was 0.892. A 2010 publication by the same authors found good reliability for automated and manual quantification of SGNF density, but poor inter- and intrareviewer reliability when using a semiquantitative approach (5-point scale).

Clinically Valid
In their 2009 report, Gibbons et al found a significant decrease in the mean SGNF density of diabetic subjects compared with controls, although there was considerable overlap in the ranges. There was also a significant association between SGNF density and neuropathy scores as measured by the Neuropathy Impairment Score in the Lower Limb, the Michigan Diabetic Neuropathy Score part 1, and the Toronto Clinical Scoring System, but not by the Michigan Neuropathy Screening Instrument. There was a moderate correlation (*r*=0.66) between SGNF density and IENF density.

Luo et al (2011) evaluated SGNF density in 35 patients with type 2 diabetes and sensory neuropathy (stocking distribution and reduced IENF density). Normative values were established in 107 control subjects, and sudomotor denervation was defined as an SGNF density less than the 5th percentile cutoff value for the sex (1.58% for men, 2.63% for women). There was no effect of age on the SGNF density. Sudomotor denervation was present in 42.86% of patients with diabetic neuropathy. The SGNF density was lower in patients with anhidrosis of the feet (0.89%) compared with patients with normal sweating (3.10%) and was not associated with autonomic symptoms in the cardiovascular, gastrointestinal, or genitourinary systems.

No studies were identified that evaluated the sensitivity or specificity of SGNF density measurement.

Clinically Useful
Analysis of SGNF density could be considered complementary to IENF density, because they assess autonomic and somatic nerves, respectively. However, no studies were identified to support an improvement in health outcomes.

Section Summary: Sweat Gland Nerve Fiber Density Measurement
The technical reliability of SGNF measurements appears to be inferior to IENF measurements, and there is considerable overlap in the ranges of SGNF density in patients with diabetic neuropathy and controls. No studies were identified that evaluated the clinical validity of SGNF density measurement. No studies were identified that showed improvements in health outcomes with SGNF density measurements.

SUMMARY OF EVIDENCE
For individuals with suspected idiopathic small fiber neuropathy who receive IENF density measurement, the evidence includes reports assessing whether IENF density measurement is technically reliable, clinically valid, and clinically useful. Relevant outcomes are test accuracy, change in disease status, symptoms, and quality of life. Techniques to measure IENF density have led to an improved understanding of the relation between the loss of small nerve fibers and symptoms of peripheral neuropathy. The literature has also indicated that low IENF density may provide supportive evidence of a lesion in the peripheral somatosensory system. For example, there is a significant decrease in average IENF density in patients diagnosed with small fiber neuropathy compared with controls, and an IENF density of 4 to 8 per mm in the calf is near the 5th percentile of normal values, suggesting an increased probability of small fiber

neuropathy below these cutoffs. For individuals who have symptoms suggestive of neuropathy but no evidence of large nerve neuropathy and no disease associated with neuropathy (eg, diabetic neuropathy, toxic neuropathy, HIV neuropathy, celiac neuropathy, inherited neuropathy), establishing a cause for the symptoms is problematic. Thus, IENF density measurement may help to diagnose idiopathic small fiber neuropathy in those who have no evidence of large fiber neuropathy and no known cause of neuropathy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have an established diagnosis of small fiber neuropathy who receive repeated IENF density measurement, the evidence is limited. Relevant outcomes are test accuracy, change in disease status, symptoms, and quality of life. A number of trials are ongoing or have recently been completed; they assess the efficacy of activity and medications on small fiber neuropathy. If successful, there might be a role for repeated IENF density measurements to result in a change in management (eg, changing dose or class of medication). However, current treatments for small fiber neuropathy only palliate symptoms and do not modify the underlying changes in nerve fiber density in patients with symptomatic neuropathy. There is no evidence that monitoring progression of neuropathy has clinical utility. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have suspected small fiber neuropathy who receive SGNF density measurement, the evidence includes comparisons with control values. Relevant outcomes are test accuracy, change in disease status, symptoms, and quality of life. Measurement of SGNF density may lead to an improved understanding of the relation between the loss of sudomotor nerve fibers and symptoms of peripheral neuropathy. However, no studies were identified that evaluated the diagnostic accuracy of SGNF density measurement. The evidence is insufficient to determine the effects of the technology on health outcomes.

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Policy History

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10/01/2009	Medical Policy Committee approval
10/14/2009	Medical Policy Implementation Committee approval. New policy.
10/14/2010	Medical Policy Committee review
10/20/2010	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/06/2011	Medical Policy Committee review
10/19/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/06/2012	Medical Policy Committee review

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09/19/2012	Medical Policy Implementation Committee approval. Coverage changed from investigational to eligible for coverage with criteria.
09/05/2013	Medical Policy Committee review
09/18/2013	Medical Policy Implementation Committee approval. "Based on review of available data, the Company considers measurement of sweat gland nerve fiber density to be investigational" was added. Intraepidermal was dropped from title.
09/04/2014	Medical Policy Committee review
09/17/2014	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2015	Coding Update
02/02/2015	Coding Update
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
09/03/2015	Medical Policy Committee review
09/23/2015	Medical Policy Implementation Committee approval. No change to coverage.
09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
09/07/2017	Medical Policy Committee review
09/20/2017	Medical Policy Implementation Committee approval. No change to coverage. Title changed.
09/06/2018	Medical Policy Committee review
09/19/2018	Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 09/2019

Coding

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

Code Type	Code
CPT	64795, 88314, 88341,88342, 88344, 88356
HCPCS	No codes
ICD-10 Diagnosis	All related diagnoses

*****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. 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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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.