MASSACHUSETTS

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Medical Policy
Nerve Fiber Density Measurement

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Policy Number: 393

BCBSA Reference Number: 2.04.58
NCD/LCD: N/A

Related Policies

Quantitative Sensory Testing, #258

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Skin biopsy with epidermal nerve fiber density measurement for the diagnosis of small-fiber neuropathy may be considered **MEDICALLY NECESSARY** when all of the following conditions are met:

1. Individual presents with symptoms of painful sensory neuropathy; AND
2. 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
3. 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
4. Electromyography and nerve-conduction studies are normal and show no evidence of large-fiber neuropathy.

Skin biopsy with epidermal nerve fiber density measurement is considered **INVESTIGATIONAL** for all other conditions, including, but not limited to, the monitoring of disease progression or response to treatment.

Measurement of sweat gland nerve fiber density is **INVESTIGATIONAL**.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO and Indemnity	Prior authorization is **not required**.
Medicare HMO Blue℠	Prior authorization is **not required**.
Medicare PPO Blue℠	Prior authorization is **not required**.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code 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 as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes

There is no specific CPT code for this service.

Description

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.

Skin Biopsy

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 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.

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 the progression of the disease and its symptoms.

Summary

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. This procedure is proposed as an objective measure of small fiber neuropathy by identifying a reduction in the density of nerve fibers.

For individuals with suspected idiopathic small fiber neuropathy who receive intraepidermal nerve fiber (IENF) density measurement, the evidence includes reports assessing whether IENF density measurement is technically reliable, clinically valid, and clinically useful. The 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 fifth 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. The 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 the 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 sweat gland nerve fiber density measurement, the evidence includes comparisons with control values. The relevant outcomes are test accuracy, change in disease status, symptoms, and quality of life. Measurement of sweat gland nerve fiber 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 sweat gland nerve fiber density measurement. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

Date	Action
1/2020	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
2/2019	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
5/2017	BCBSA National medical policy review.

	New investigational indications described. Title changed. Effective 5/1/2017.
12/2014	New references added from BCBSA National medical policy.
1/2014	New references added from BCBSA National medical policy.
11/1/12	New policy describing ongoing coverage and non-coverage.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

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