Medical Policy
Nerve Fiber Density Testing

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Policy Number: 393
BCBSA Reference Number: 2.04.58

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.

Prior Authorization Information
Commercial Members: Managed Care (HMO and POS)
Prior authorization is **NOT** required.

Commercial Members: PPO, and Indemnity
Prior authorization is **NOT** required.

Medicare Members: HMO Blue℠
Prior authorization is **NOT** required.
Medicare Members: PPO BlueSM

Prior authorization is NOT required.

CPT Codes / HCPCS Codes / ICD-9 Codes
The following codes are included below for informational purposes. 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 procedure code for this service.

Description
The majority of 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 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. Small fiber neuropathy occurs most often in patients with diabetic neuropathy but may also be found in patients with impaired glucose tolerance, severe hypertriglyceridemia, the metabolic syndrome, human immunodeficiency virus (HIV) infection, and toxic neuropathy from antiretroviral drugs. For many patients, no specific etiology is identified.

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. In addition, conditions other than nerve fiber damage, including venous insufficiency, spinal stenosis, myelopathy, and psychosomatic disturbances may mimic small fiber neuropathy. There is no treatment to cure small fiber peripheral neuropathy. Medications may be provided for pain management, and for some etiologies, treatment of the underlying condition (e.g., glucose control, intravenous immunoglobulin or plasma exchange) may be given to reduce progression of the disease and its symptoms.

In the last decade, a specific test to assess intraepidermal nerve fiber (IENF) density using skin biopsy and immunostaining of the tissue has been developed that allows the identification and counting of intraepidermal nerve fibers. Assessment of IENF 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.

Summary
Overall, a number of questions remain about whether a quantitative assessment of IENF density results in improved health outcomes. Additional prospective studies are needed to evaluate the effect of this procedure in comparison with clinical diagnosis alone in patients with known causes of neuropathy. For this reason, IENF density measurement may be considered medically necessary in patients with suspected idiopathic small fiber neuropathy when the 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. Assessment of IENF density in all other conditions is considered investigational.

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, evidence is insufficient to permit conclusions regarding the impact of measurement of SGNF density on health outcomes. Measurement of SGNF density is considered investigational.

Policy History

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<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>1/2014</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>11/1/12</td>
<td>New policy describing ongoing coverage and non-coverage</td>
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</table>

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

References