

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

Medical Policy Nerve Fiber Density Testing

Table of Contents

- Policy: Commercial
- Policy: Medicare
- <u>Authorization Information</u>
- <u>Coding Information</u>
- Description
- Policy History
- Information Pertaining to All Policies
- References

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 BlueSM and Medicare PPO BlueSM 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 <u>INVESTIGATIONAL</u> 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 BlueSM

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

Date	Action
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

References

- 1. Lauria G, Cornblath DR, Johansson O et al. EFNS guidelines on the use of skin biopsy in the diagnosis of peripheral neuropathy. Eur J Neurol 2005; 12(10):747-58.
- Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on the use of skin biopsy in the diagnosis of small fiber neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. J Peripher Nerv Syst 2010; 15(2):79-92.
- 3. England JD, Gronseth GS, Franklin G et al. Practice Parameter: evaluation of distal symmetric polyneuropathy: role of autonomic testing, nerve biopsy, and skin biopsy (an evidence-based review). Report of the American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation. Neurology 2009; 72(2):177-84.
- 4. McArthur JC, Stocks EA, Hauer P et al. Epidermal nerve fiber density: normative reference range and diagnostic efficiency. Arch Neurol 1998; 55(12):1513-20.
- 5. Holland NR, Stocks A, Hauer P et al. Intraepidermal nerve fiber density in patients with painful sensory neuropathy. Neurology 1997; 48(3):708-11.
- Handelsman Y, Mechanick JI, Blonde L et al; AACE Task Force for Developing Diabetes Comprehensive Care Plan. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Developing a Diabetes Mellitus Comprehensive Care Plan. Endocr Pract 2011; 17 Suppl 2:1-53. Available online at: https://www.aace.com/files/dm-guidelines-ccp.pdf. Last accessed August, 2013.
- 7. Periquet MI, Novak V, Collins MP et al. Painful sensory neuropathy: prospective evaluation using skin biopsy. Neurology 1999; 53(8):1641-7.
- Walk D, Wendelschafer-Crabb G, Davey C et al. Concordance between epidermal nerve fiber density and sensory examination in patients with symptoms of idiopathic small fiber neuropathy. J Neurol Sci 2007; 255(1-2):23-6.
- 9. Walk D. Role of skin biopsy in the diagnosis of peripheral neuropathic pain. Curr Pain Headache Rep 2009; 13(3):191-6.
- 10. Devigili G, Tugnoli V, Penza P et al. The diagnostic criteria for small fibre neuropathy: from symptoms to neuropathology. Brain 2008; 131(Pt 7):1912-25.
- 11. Scherens A, Maier C, Haussleiter IS et al. Painful or painless lower limb dysesthesias are highly predictive of peripheral neuropathy: comparison of different diagnostic modalities. Eur J Pain 2009; 13(7):711-8.

- 12. Krishnan ST, Quattrini C, Jeziorska M et al. Abnormal LDIflare but normal quantitative sensory testing and dermal nerve fiber density in patients with painful diabetic neuropathy. Diabetes Care 2009; 32(3):451-5.
- 13. Bakkers M, Merkies IS, Lauria G et al. Intraepidermal nerve fiber density and its application in sarcoidosis. Neurology 2009; 73(14):1142-8.
- 14. Nebuchennykh M, Loseth S, Lindal S et al. The value of skin biopsy with recording of intraepidermal nerve fiber density and quantitative sensory testing in the assessment of small fiber involvement in patients with different causes of polyneuropathy. J Neurol 2009; 256(7):1067-75.
- 15. Lauria G, Bakkers M, Schmitz C et al. Intraepidermal nerve fiber density at the distal leg: a worldwide normative reference study. J Peripher Nerv Syst 2010; 15(3):202-7.
- 16. Boruchow SA, Gibbons CH. The utility of skin biopsy in management of small fiber neuropathy. Muscle Nerve 2013.
- 17. Kles KA, Bril V. Diagnostic tools for diabetic sensorimotor polyneuropathy. Curr Diabetes Rev 2006; 2(3):353-61.
- 18. Hovaguimian A, Gibbons CH. Diagnosis and Treatment of Pain in Small-fiber Neuropathy. Curr Pain Headache Rep 2011; 15(3):193-200.
- 19. Gibbons CH, Illigens BM, Wang N et al. Quantification of sweat gland innervation: a clinicalpathologic correlation. Neurology 2009; 72(17):1479-86.
- 20. Gibbons CH, Illigens BM, Wang N et al. Quantification of sudomotor innervation: a comparison of three methods. Muscle Nerve 2010; 42(1):112-9.
- 21. Luo KR, Chao CC, Chen YT et al. Quantitation of sudomotor innervation in skin biopsies of patients with diabetic neuropathy. J Neuropathol Exp Neurol 2011; 70(10):930-8.
- 22. Alport AR, Sander HW. Clinical approach to peripheral neuropathy: anatomic localization and diagnostic testing. Continuum (Minneap Minn) 2012; 18(1):13-38.
- 23. Jacobs AM, Cheng D. Management of diabetic small-fiber neuropathy with combination Lmethylfolate, methylcobalamin, and pyridoxal 5'-phosphate. Rev Neurol Dis 2011; 8(1-2):39-47.
- 24. England JD, Gronseth GS, Franklin G et al. Evaluation of distal symmetric polyneuropathy: the role of autonomic testing, nerve biopsy, and skin biopsy (an evidence-based review). Muscle Nerve 2009; 39(1):106-15.
- Centers for Medicare and Medicaid. NCD for Services Provided for the Diagnosis and Treatment of Diabetic Sensory NEUROPATHY with Loss of Protective Sensation (aka Diabetic Peripheral NEUROPATHY) (70.2.1). 2002. Available online at:

http://www.cms.gov/mcd/viewncd.asp?ncd_id=70.2.1&ncd_version=1&basket=ncd%3A70%2E2%2 E1%3A1%3AServices+Provided+for+the+Diagnosis+and+Treatment+of+Diabetic+Sensory+Neurop athy+with+Loss+of+Protective+Sensation+%28aka+Diabetic+Peripheral+Neuropathy%29. Last accessed August, 2013.