

Reimbursement Policy

Nerve Fiber Density Testing

[POLICY DESCRIPTION](#) | [INDICATIONS AND/OR LIMITATIONS OF COVERAGE](#) | [APPLICABLE STATE AND FEDERAL REGULATIONS](#) | [APPLICABLE CPT/HCPCS PROCEDURE CODES](#) | [EVIDENCE-BASED SCIENTIFIC REFERENCES](#) | [REVISION HISTORY](#)

I. Policy Description

Nerve fiber density testing involves analysis of skin biopsy stained with an antibody to antiprotein gene product 9.5¹ which avidly stains all axons.² The number and morphology of axons within the epidermis are evaluated to determine epidermal nerve fiber density³ and assess for the presence and degree of neuropathy.⁴

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the "Applicable State and Federal Regulations" section of this policy document.

- 1) For the diagnosis of small-fiber neuropathy, epidermal nerve fiber density measurement from a skin biopsy **MEETS COVERAGE CRITERIA** when **all** of the following conditions are met:
 - a) An individual presents with symptoms of painful sensory neuropathy;
 - b) 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);
 - c) 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;
 - d) Electromyography and nerve-conduction studies are normal and show no evidence of large-fiber neuropathy.
- 2) For all other situations not described above, epidermal nerve fiber density measurement from a skin biopsy **DOES NOT MEET COVERAGE CRITERIA**.
- 3) Measurement of sweat gland nerve fiber density **DOES NOT MEET COVERAGE CRITERIA**.

III. Applicable State and Federal Regulations

DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please

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visit the Medicare search website: <https://www.cms.gov/medicare-coverage-database/search.aspx>. For the most up-to-date Medicaid policies and coverage, visit the applicable state Medicaid website.

Food and Drug Administration (FDA)

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

IV. Applicable CPT/HCPCS Procedure Codes

CPT	Code Description
88313	Special stain including interpretation and report; Group II, all other (eg, iron, trichrome), except stain for microorganisms, stains for enzyme constituents, or immunocytochemistry and immunohistochemistry
88341	Immunohistochemistry or immunocytochemistry, per specimen; each additional single antibody stain procedure (List separately in addition to code for primary procedure)
88342	Immunohistochemistry or immunocytochemistry, per specimen; initial single antibody stain procedure
88344	Immunohistochemistry or immunocytochemistry, per specimen; each multiplex antibody stain procedure
88346	Immunofluorescence, per specimen; initial single antibody stain procedure
88350	Immunofluorescence, per specimen; each additional single antibody stain procedure (List separately in addition to code for primary procedure)
88356	Morphometric analysis; nerve

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Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

V. Evidence-based Scientific References

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VI. Revision History

Revision Date	Summary of Changes
12/03/2025	Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate any modifications to coverage criteria.