

Policy: MP352

Section: Medical Policy

Subject: Epidermal Nerve Fiber Density Testing

Applicable Lines of Business

Commercial	X	CHIP	X
Medicare	X	ACA	X
Medicaid	X		

I. Policy: Epidermal Nerve Fiber Density Testing

II. Purpose/Objective:

To provide a policy of coverage regarding Nerve Fiber Density Testing

III. Responsibility:

- A. Medical Directors
- B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

- a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
- b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
- c. in accordance with current standards of good medical treatment practiced by the general medical community.
- d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
- e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment

Medically Necessary — A service, item, procedure, or level of care that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

- Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
- Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an

illness, condition, injury or disability.

- Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age

DESCRIPTION:

Epidermal Nerve Fiber Density (ENFD) Testing is based on the analysis of a punch biopsy of skin and is used to assist in the diagnosis of small fiber neuropathy. Small fiber peripheral neuropathy may be caused by a wide array of medical conditions or exposures. It has been long known that the most common causes are diabetes mellitus (types I and II) and idiopathic.

INDICATIONS:

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:

- The member presents with symptoms of painful sensory neuropathy; **and**
- There is no confounding disorder known to be the etiology of 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 (e.g. reduced or absent muscle-stretch reflexes; reduced proprioception and /or vibratory sensation); **and**
- Electromyography (EMG) and nerve-conduction studies show no evidence of large-fiber neuropathy.

EXCLUSIONS:

Skin biopsy with epidermal nerve fiber density measurement for conditions other than those listed under Indication are considered **Experimental, Investigational or Unproven** and are **NOT COVERED**.

Skin biopsy with epidermal nerve fiber density measurement for the purpose of determination of treatment response or monitoring of disease progression is considered **Experimental, Investigational or Unproven** and is **NOT COVERED**.

Skin biopsy with sweat gland nerve fiber density measurement is considered **Experimental, Investigational or Unproven** and is **NOT COVERED**.

Medicaid Business Segment:

Any requests for services, that do not meet criteria set in the PARP, may be evaluated on a case by case basis.

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

CODING ASSOCIATED WITH:

The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.

- 11104 Punch biopsy of skin (including simple closure, when performed); single lesion
- 11105 Punch biopsy of skin (including simple closure, when performed); each separate/additional lesion
- 88305 Level IV Surgical pathology, gross and microscopic examination, nerve, biopsy
- 88314 Special stain including interpretation and report; histochemical stain on frozen tissue block
- 88356 Morphometric analysis; nerve [when specified as analysis of intra-epidermal nerve fiber density]
- 88399 Unlisted surgical pathology procedure [when specified as analysis of intra-epidermal nerve fiber density]

LINE OF BUSINESS:

Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

REFERENCES:

Boruchow SA, Gibbons CH. Utility of skin biopsy in management of small fiber neuropathy. *Muscle Nerve*. 2013; 48(6):877-882

Koskinen M, Hietaharju A, Kylaniemi M, et al. A quantitative method for the assessment of intraepidermal nerve fibers in small-fiber neuropathy. *J Neurol*. 2005; 252(7):789-794.

Collongues, N., Samama, B., et al. Quantitative and qualitative normative dataset for intraepidermal nerve fibers using skin biopsy. *PLoS One*, 2018;13(1), e0191614.

Pittenger G, Ray M, Burcus NI, et al. Intraepidermal nerve fibers are indicators of small-fiber neuropathy in both diabetic and non-diabetic patients. *Diabetes Care*. 2004; 27(8): 1974-1979.

Cazzato, D., Castori, M., et al. Small fiber neuropathy is a common feature of Ehlers-Danlos syndromes. *Neurology*, 2016;87(2), 155-159

Gibbons, C. H., Griffin, J. W., et al. The utility of skin biopsy for prediction of progression in suspected small fiber neuropathy. *Neurology*, 2006; 66(2), 256-258.

Gibbons, C. H., Illigens, B. M., et al. Quantification of sweat gland innervation: a clinical-pathologic correlation. *Neurology*, 2009;72(17), 1479-1486

Saperstein DS, Levine TD, Levine M, Hank N. Usefulness of skin biopsies in the evaluation and management of patients with suspected small fiber neuropathy. *Int J Neurosci*. 2013; 123(1):38-41.

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*. Jan 13 2009; 72(2): 177-84

Centers for Medicare & Medicaid. National Coverage Determination (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).

Devigili, G., Rinaldo, S., et al. Diagnostic criteria for small fiber neuropathy in clinical practice and research. *Brain*, 2019;142(12), 3728-3736

Alam, U., Jeziorska, M., et al.. Diagnostic utility of corneal confocal microscopy and intra-epidermal nerve fibre density in diabetic neuropathy. *PLoS One*, 2017;12(7), e0180175

Provitera, V., Gibbons, C. H. et al. The role of skin biopsy in differentiating small-fiber neuropathy from ganglionopathy. *Eur J Neurol*, 2018;25(6), 848-853.

Vlckova-Moravcova, E., Bednarik, J., et al. Diagnostic validity of epidermal nerve fiber densities in painful sensory neuropathies. *Muscle Nerve*, 2008;37(1), 50-60.

Caro, X. J., Winter, E. F. Evidence of abnormal epidermal nerve fiber density in fibromyalgia: clinical and immunologic implications. *Arthritis Rheumatol*, 2014;66(7), 1945-1954

Piscosquito, G., Provitera, V., et al. The analysis of epidermal nerve fibre spatial distribution improves the diagnostic yield of skin biopsy. *Neuropathology and Applied Neurobiology*, 2021;47(2), 210-217.

Haroutounian S, Todorovic MS, Leinders M, et al. Diagnostic criteria for idiopathic small fiber neuropathy: A systematic review. *Muscle Nerve*. 2021;63(2):170-177.

This policy will be revised as necessary and reviewed no less than annually.

Devised: 11/21

Revised:

Reviewed: 12/22, 12/23

Geisinger Health Plan may refer collectively to health care coverage sponsors Geisinger Health Plan, Geisinger Quality Options, Inc., and Geisinger Indemnity Insurance Company, unless otherwise noted. Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Coverage for experimental or investigational treatments, services and procedures is specifically excluded under the member's certificate with Geisinger Health Plan. Unproven services outside of an approved clinical trial are also specifically excluded under the member's certificate with Geisinger Health Plan. This policy does not expand coverage to services or items specifically excluded from coverage in the member's certificate with Geisinger Health Plan. Additional information can be found in MP015 Experimental, Investigational or Unproven Services.

Prior authorization and/or pre-certification requirements for services or items may apply. Pre-certification lists may be found in the member's contract specific benefit document. Prior authorization requirements can be found at <https://www.geisinger.org/health-plan/providers/ghp-clinical-policies>

Please be advised that the use of the logos, service marks or names of Geisinger Health Plan, Geisinger Quality Options, Inc. and Geisinger Indemnity Insurance Company on a marketing, press releases or any communication piece regarding the contents of this medical policy is strictly prohibited without the prior written consent of Geisinger Health Plan. Additionally, the above medical policy does not confer any endorsement by Geisinger Health Plan, Geisinger Quality Options, Inc. and Geisinger Indemnity Insurance Company regarding the medical service, medical device or medical lab test described under this medical policy.