THE OHIO STATE UNIVERSITY
HEALTH PLAN

Subject: Intraepidermal Nerve Fiber Density Assessment **Revision Date:** 12/25

DESCRIPTION

According to the AAN, AANEM, and AAPM&R, distal symmetric polyneuropathy (DSP) is the most common variety of neuropathy. Since there are many etiologies of polyneuropathy, a logical clinical approach is needed for evaluation and management. Skin biopsy is being increasingly used to evaluate patients with polyneuropathy. The most common technique involves a 3 mm punch biopsy of skin from the leg. 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 staining allows for the identification and counting of intraepidermal nerve fibers (IENF). IENF density assessment using PGP 9.5 immnohistochemistry is a validated, reproducible marker of small fiber sensory pathology. Skin biopsy with IENF density assessment is useful to identify DSP which includes SFSN in symptomatic patients with suspected polyneuropathy.

APPLICABILITY

This policy applies to all OSU Health Plan (OSUHP) benefit plans.

DEFINITIONS

Distal symmetric polyneuropathy is a nerve condition that causes numbness, tingling, or pain in both feet or hands, usually starting in the toes and fingers and slowly spreading upward.

Immunohistochemical method is a lab test that uses special stains to detect specific proteins in tissue samples, helping doctors diagnose certain diseases or conditions.

Immunofluorescent method is a lab test that uses glowing dyes to find specific proteins in tissue, helping doctors diagnose certain diseases or conditions.

Immunostained means a tissue sample has been treated with special dyes to highlight certain proteins, helping doctors see signs of disease.

Intraepidermal nerve fibers are tiny nerves in the outer layer of the skin that help you feel things like touch, pain, and temperature.

Polyneuropathy is a condition where many nerves throughout the body are damaged, causing symptoms like numbness, tingling, weakness, or pain—usually starting in the hands or feet.

Punch biopsy is a quick procedure where a small, round piece of skin is removed to check for disease.

POLICY

The OSU Health Plan considers IENF density assessment medically necessary when ALL the following criteria are met:

- Symptoms of small fiber neuropathy are present (distal burning, pain, numbness and paresthesias); 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 have been performed and are normal (no evidence of large-fiber neuropathy).

PROCEDURE

OSU Health Plan will authorize Intraepidermal Nerve Fiber Density Assessment when the above criteria have been met.

PRIOR AUTHORIZATION

Prior authorization is required.

EXCLUSIONS

The OSU Health Plan considers measurement of IENF density experimental and investigational for monitoring disease progression or response to treatment, or for the following indications (not an all- inclusive list):

- As a marker of pre-clinical asymptomatic small-fiber sensory neuropathy in hypothyroid patients
- Evaluation of individuals with Ehlers-Danlos syndromes
- Evaluation of individuals with Fabry disease
- Evaluation of individuals with fibromyalgia (when above criteria for small fiber neuropathy are not met)
- Evaluation of individuals with postural tachycardia syndrome
- Evaluation of individuals with REM sleep behavior disorder
- Diagnosis of endometriosis
- Evaluation of hereditary transthyretin (TTR) amyloidosis and iatrogenic TTR amyloidosis

Measurement of sweat gland nerve fiber density for the diagnosis of complex regional pain syndrome, small-fiber neuropathy and other indications is considered experimental and investigational because its effectiveness has not been established.

CODES

There are no specific codes for Intra-Epidermal Nerve Fiber Density Measurement. Specific CPT codes listed in this policy are based on coding by Corinthian Reference Lab.

CPT codes covered if selection criteria are met:

CPT code	**Description**

10004	Fine needle aspiration biopsy, without imaging guidance; each additional lesion (List separately in addition to code for primary procedure)
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 (List separately in addition to code for primary procedure)
88305	Level IV – Surgical pathology, gross and microscopic examination
88314	Histochemical stain on frozen tissue block (List separately in addition to code for primary procedure)
88341-88344	Immunohistochemistry or immunocytochemistry, per specimen
88356	Morphometric analysis; nerve
95860-95872	Electromyography
95907-95913	Nerve conduction studies
95921-95923	Testing of autonomic nervous system function
95937	Neuromuscular junction testing (repetitive stimulation, paired stimuli), each nerve, any 1 method

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