



Subject: Intraepidermal Nerve Fiber Density Assessment

Revision Date: 6/24

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 immunohistochemistry is a validated, reproducible marker of small fiber sensory pathology. Skin biopsy with IENF density assessment is possibly useful to identify DSP which includes SFSN in symptomatic patients with suspected polyneuropathy.

POLICY

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

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

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.

PRIOR AUTHORIZATION

Prior authorization is required.

RELATED CPT/HCPC 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:

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)
88342	Immunohistochemistry or immunocytochemistry, per specimen; initial single antibody stain procedure
88341	Each additional single antibody stain procedure (List separately in addition to code for primary procedure)
88356	Morphometric analysis; nerve

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