



Subject: Intraepidermal Nerve Fiber Density Assessment Policy

Effective Date: 5/16

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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
- Evaluation of individuals with postural tachycardia syndrome
- Evaluation of individuals with REM sleep behavior disorder

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

REFERENCES

- Aetna. (2017). Nerve fiber density measurement. Retrieved from http://www.aetna.com/cpb/medical/data/700_799/0774.html
- Anthem. (2018). Skin nerve fiber density testing. Retrieved from https://www.anthem.com/medicalpolicies/guidelines/gl_pw_d080195.htm
- Crucci, G., et al. (2010). EFNS guidelines on neuropathic pain assessment: Revised 2009. *European Journal of Neurology*, 17, 1010-1018. DOI: 10.1111/j.1468-1331.2010.02969.x
- England, J. D., Gronseth, G. S., Franklin, G., et al. (2009). 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*, 72, 177-184.
- European Federation of Neurological Societies/Peripheral Nerve Society Joint Task Force of the EFNS and the PNS. (2010). 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*, 15(2),79-92.
- Health Net. (2016). Intraepidermal nerve fiber density testing in the diagnosis of small fiber neuropathy. Retrieved from <https://www.healthnet.com/static/general/unprotected/pdfs/national/policies/IntraepidermalNerveFiberDensityTesting.pdf>
- Rutkove, S. B. (2015). Overview of polyneuropathy. *UpToDate*. Retrieved from http://www.uptodate.com/contents/overview-of-polyneuropathy?source=search_result&search=intra-epidermal+nerve+fiber+density+skin+testing&selectedTitle=1~150