

If a conflict arises between a Clinical Payment and Coding Policy and any plan document under which a member is entitled to Covered Services, the plan document will govern. If a conflict arises between a CPCP and any provider contract pursuant to which a provider participates in and/or provides Covered Services to eligible member(s) and/or plans, the provider contract will govern. "Plan documents" include, but are not limited to, Certificates of Health Care Benefits, benefit booklets, Summary Plan Descriptions, and other coverage documents. Blue Cross and Blue Shield of Oklahoma may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSOK has full and final discretionary authority for their interpretation and application to the extent provided under any applicable plan documents.

Providers are responsible for submission of accurate documentation of services performed. Providers are expected to submit claims for services rendered using valid code combinations from Health Insurance Portability and Accountability Act approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing Editor, American Medical Association, Current Procedural Terminology, CPT® Assistant, Healthcare Common Procedure Coding System, ICD-10 CM and PCS, National Drug Codes, Diagnosis Related Group guidelines, Centers for Medicare and Medicaid Services National Correct Coding Initiative Policy Manual, CCI table edits and other CMS guidelines.

Claims are subject to the code edit protocols for services/procedures billed. Claim submissions are subject to claim review including but not limited to, any terms of benefit coverage, provider contract language, medical policies, clinical payment and coding policies as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

Nerve Fiber Density Testing

Policy Number: CPCPLAB064

Version 1.0

Approval Date: Jan. 12, 2026

Plan Effective Date: May 1, 2026

Description

The Plan has implemented certain lab management reimbursement criteria. Not all requirements apply to each product. Providers are urged to review Plan documents for eligible coverage for services rendered.

Reimbursement Information:

1. For the diagnosis of small-fiber neuropathy, epidermal nerve fiber density measurement from a skin biopsy **may be reimbursable** 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 **is not reimbursable**.
3. Measurement of sweat gland nerve fiber density **is not reimbursable**.

Procedure Codes

The following is not an all-encompassing code list. The inclusion of a code does not guarantee that it is a covered service or eligible for reimbursement.

Codes
88313, 88341, 88342, 88344, 88346, 88350, 88356

References:

1. Wilkinson KD, Lee KM, Deshpande S, Duerksen-Hughes P, Boss JM, Pohl J. The neuron-specific protein PGP 9.5 is a ubiquitin carboxyl-terminal hydrolase. *Science (New York, NY)*. Nov 03 1989;246(4930):670-3. doi:10.1126/science.2530630
2. Dalsgaard CJ, Rydh M, Haegerstrand A. Cutaneous innervation in man visualized with protein gene product 9.5 (PGP 9.5) antibodies. *Histochemistry*. 1989;92(5):385-90. doi:10.1007/BF00492495
3. McCarthy BG, Hsieh ST, Stocks A, et al. Cutaneous innervation in sensory neuropathies: evaluation by skin biopsy. *Neurology*. Oct 1995;45(10):1848-55. doi:10.1212/wnl.45.10.1848

4. Smith AG, Gibson S. Skin biopsy for the evaluation of peripheral nerve disease. Updated January 30, 2025. <https://www.uptodate.com/contents/skin-biopsy-for-the-evaluation-of-peripheral-nerve-disease>
5. Chien HF, Tseng TJ, Lin WM, et al. Quantitative pathology of cutaneous nerve terminal degeneration in the human skin. *Acta neuropathologica*. Nov 2001;102(5):455-61. doi:10.1007/s004010100397
6. Lauria G, Devigili G. Skin biopsy as a diagnostic tool in peripheral neuropathy. *Nature clinical practice Neurology*. Oct 2007;3(10):546-57. doi:10.1038/ncpneuro0630
7. Therapath. Small Fiber Neuropathy Testing. <https://www.therapath.com/services/small-fiber-neuropathy-testing/>
8. BakoDx. Epidermal Nerve Fiber Density (ENFD) Testing. <https://bakodx.com/enfd/>
9. Ipsum Diagnostics. Nerve Testing. 2022;
10. CRL. Small Fiber Neuropathy is Painful. Diagnosing it Shouldn't Be. <https://corinthianreferencelab.com/>
11. 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). *Neurology*. 2009;72(2):177. doi:10.1212/01.wnl.0000336345.70511.0f
12. Collongues N, Samama B, Schmidt-Mutter C, et al. Quantitative and qualitative normative dataset for intraepidermal nerve fibers using skin biopsy. *PloS one*. 2018;13(1):e0191614. doi:10.1371/journal.pone.0191614
13. Piscosquito G, Provitera V, Mozzillo S, 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. doi:10.1111/nan.12651
14. Corrà MF, Sousa M, Reis I, et al. Advantages of an Automated Method Compared With Manual Methods for the Quantification of Intraepidermal Nerve Fiber in Skin Biopsy. *J Neuropathol Exp Neurol*. Aug 11 2021;80(7):685-694. doi:10.1093/jnen/nlab045
15. McArthur JC, Stocks EA, Hauer P, Cornblath DR, Griffin JW. Epidermal nerve fiber density: normative reference range and diagnostic efficiency. *Archives of neurology*. Dec 1998;55(12):1513-20. doi:10.1001/archneur.55.12.1513
16. Devigili G, Tugnoli V, Penza P, et al. The diagnostic criteria for small fibre neuropathy: from symptoms to neuropathology. *Brain : a journal of neurology*. Jul 2008;131(Pt 7):1912-25. doi:10.1093/brain/awn093
17. Devigili G, Rinaldo S, Lombardi R, et al. Diagnostic criteria for small fibre neuropathy in clinical practice and research. *Brain : a journal of neurology*. Dec 1 2019;142(12):3728-3736. doi:10.1093/brain/awz333
18. Vlckova-Moravcova E, Bednarik J, Dusek L, Toyka KV, Sommer C. Diagnostic validity of epidermal nerve fiber densities in painful sensory neuropathies. *Muscle & nerve*. Jan 2008;37(1):50-60. doi:10.1002/mus.20889
19. Gibbons CH, Griffin JW, Polydefkis M, et al. The utility of skin biopsy for prediction of progression in suspected small fiber neuropathy. *Neurology*. Jan 24 2006;66(2):256-8. doi:10.1212/01.wnl.0000194314.86486.a2
20. Gibbons CH, Illigens BM, Wang N, Freeman R. Quantification of sweat gland innervation: a clinical-pathologic correlation. *Neurology*. Apr 28 2009;72(17):1479-86. doi:10.1212/WNL.0b013e3181a2e8b8

21. Luo KR, Chao CC, Chen YT, et al. Quantitation of sudomotor innervation in skin biopsies of patients with diabetic neuropathy. *J Neuropathol Exp Neurol*. Oct 2011;70(10):930-8. doi:10.1097/NEN.0b013e318230b0f4
22. Hovaguimian A, Gibbons CH. Clinical Approach to the Treatment of Painful Diabetic Neuropathy. *Ther Adv Endocrinol Metab*. Feb 2011;2(1):27-38. doi:10.1177/2042018810391900
23. Callaghan BC, Xia R, Reynolds E, et al. Association Between Metabolic Syndrome Components and Polyneuropathy in an Obese Population. *JAMA neurology*. Dec 1 2016;73(12):1468-1476. doi:10.1001/jamaneurol.2016.3745
24. Callaghan BC, Gao L, Li Y, et al. Diabetes and obesity are the main metabolic drivers of peripheral neuropathy. *Annals of clinical and translational neurology*. Apr 2018;5(4):397-405. doi:10.1002/acn3.531
25. Alam U, Jeziorska M, Petropoulos IN, et al. Diagnostic utility of corneal confocal microscopy and intra-epidermal nerve fibre density in diabetic neuropathy. *PloS one*. 2017;12(7):e0180175. doi:10.1371/journal.pone.0180175
26. Wang M, Zhang C, Zuo A, Li L, Chen L, Hou X. Diagnostic utility of corneal confocal microscopy in type 2 diabetic peripheral neuropathy. *Journal of Diabetes Investigation*. 2021;12(4):574-582. doi:10.1111/jdi.13381
27. Chao CC, Huang CM, Chiang HH, et al. Sudomotor innervation in transthyretin amyloid neuropathy: Pathology and functional correlates. *Annals of neurology*. Aug 2015;78(2):272-83. doi:10.1002/ana.24438
28. Mantyh WG, Dyck PJ, Engelstad JK, Litchy WJ, Sandroni P, Davis MD. Epidermal Nerve Fiber Quantification in Patients With Erythromelalgia. *JAMA dermatology*. Dec 7 2016;doi:10.1001/jamadermatol.2016.4404
29. Caro XJ, Winter EF. Evidence of abnormal epidermal nerve fiber density in fibromyalgia: clinical and immunologic implications. *Arthritis & rheumatology (Hoboken, NJ)*. Jul 2014;66(7):1945-54. doi:10.1002/art.38662
30. Lawson VH, Grewal J, Hackshaw KV, Mongiovi PC, Stino AM. Fibromyalgia syndrome and small fiber, early or mild sensory polyneuropathy. *Muscle & nerve*. Mar 23 2018;doi:10.1002/mus.26131
31. Evdokimov D, Dinkel P, Frank J, Sommer C, Üçeyler N. Characterization of dermal skin innervation in fibromyalgia syndrome. *PloS one*. 2020;15(1):e0227674. doi:10.1371/journal.pone.0227674
32. Provitera V, Gibbons CH, Wendelschafer-Crabb G, et al. The role of skin biopsy in differentiating small-fiber neuropathy from ganglionopathy. *Eur J Neurol*. Jun 2018;25(6):848-853. doi:10.1111/ene.13608
33. Magri F, Buonocore M, Oliviero A, et al. Intraepidermal nerve fiber density reduction as a marker of preclinical asymptomatic small-fiber sensory neuropathy in hypothyroid patients. *European journal of endocrinology*. Aug 2010;163(2):279-84. doi:10.1530/eje-10-0285
34. Gupta N, Arora M, Sharma R, Arora KS. Peripheral and Central Nervous System Involvement in Recently Diagnosed Cases of Hypothyroidism: An Electrophysiological Study. *Annals of medical and health sciences research*. Sep-Oct 2016;6(5):261-266. doi:doi.org/10.4103/amhsr.amhsr_39_16
35. Torvin Moller A, Winther Bach F, Feldt-Rasmussen U, et al. Functional and structural nerve fiber findings in heterozygote patients with Fabry disease. *Pain*. Sep 2009;145(1-2):237-45. doi:10.1016/j.pain.2009.06.032

36. van der Tol L, Verhamme C, van Schaik IN, van der Kooi AJ, Hollak CE, Biegstraaten M. In Patients with an alpha-Galactosidase A Variant, Small Nerve Fibre Assessment Cannot Confirm a Diagnosis of Fabry Disease. *JIMD reports*. 2016;28:95-103. doi:10.1007/8904_2015_503
37. von Cossel K, Muschol N, Friedrich RE, et al. Assessment of small fiber neuropathy in patients carrying the non-classical Fabry variant p.D313Y. *Muscle & nerve*. 2021;63(5):745-750. doi:10.1002/mus.27196
38. Jeziorska M, Atkinson A, Kass-Iliyya L, et al. Increased Intraepidermal Nerve Fiber Degeneration and Impaired Regeneration Relate to Symptoms and Deficits in Parkinson's Disease. *Frontiers in neurology*. 2019;10:111. doi:10.3389/fneur.2019.00111
39. Lim SH, Ferdousi M, Kalteniece A, et al. Corneal Confocal Microscopy Identifies Parkinson's Disease with More Rapid Motor Progression. *Movement Disorders*. 2021;n/a(n/a)doi:10.1002/mds.28602
40. Duchesne M, Danigo A, Richard L, et al. Skin Biopsy Findings in Patients With CMT1A: Baseline Data From the CLN-PXT3003-01 Study Provide New Insights Into the Pathophysiology of the Disorder. *J Neuropathol Exp Neurol*. Apr 1 2018;77(4):274-281. doi:10.1093/jnen/nly001
41. Cazzato D, Castori M, Lombardi R, et al. Small fiber neuropathy is a common feature of Ehlers-Danlos syndromes. *Neurology*. Jul 12 2016;87(2):155-9. doi:10.1212/wnl.0000000000002847
42. Indelicato E, Nachbauer W, Eigentler A, Rudzki D, Wanschitz J, Boesch S. Intraepidermal Nerve Fiber Density in Friedreich's Ataxia. *J Neuropathol Exp Neurol*. Dec 1 2018;77(12):1137-1143. doi:10.1093/jnen/nly100
43. Bandinelli F, Carlo MD, Colantuono VA, et al. Post-COVID-19 Small Fiber Neuropathy as a New Emerging Quality of Life-Threatening Disease: A Systematic Review. *Microorganisms*. 2025;(2025;13(2):328)doi:10.3390/microorganisms13020328
44. Abrams RMC, Simpson DM, Navis A, Jette N, MD LZ, Shin SC. Small fiber neuropathy associated with SARS-CoV-2 infection. *Muscle & nerve*. 2022;doi:10.1002/mus.27458
45. Azcue N, Teijeira-Portas S, Tijero-Merino B, et al. Small fiber neuropathy in the post-COVID condition and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Clinical significance and diagnostic challenges. *Eur J Neurol*. 2025;32(2)doi:10.1111/ene.70016
46. Gavrilova N, Starshinova A, Zinchenko Y, et al. Small Fiber Neuropathy in Sarcoidosis. *Pathophysiology*. Dec 20 2021;28(4):544-550. doi:10.3390/pathophysiology28040035
47. England JD, Gronseth GS, Franklin G, et al. Practice Parameter: evaluation of distal symmetric polyneuropathy: role of laboratory and genetic testing (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):185-92. doi:10.1212/01.wnl.0000336370.51010.a1
48. AAN. Evaluation of Distal Symmetric Polyneuropathy: Role of Autonomic Testing, Nerve Biopsy, and Skin Biopsy American Academy of Neurology. Updated February 8, 2025. <https://www.aan.com/Guidelines/home/GuidelineDetail/315>

49. Garber AJ, Abrahamson MJ, Barzilay JI, et al. AACE/ACE comprehensive diabetes management algorithm 2015. *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*. Apr 2015;21(4):438-47. doi:10.4158/ep15693.cs
50. EFNS. European Federation of Neurological Societies/Peripheral Nerve Society 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. *Journal of the peripheral nervous system : JPNS*. Jun 2010;15(2):79-92. doi:10.1111/j.1529-8027.2010.00269.x
51. Shun CT, Chang YC, Wu HP, et al. Skin denervation in type 2 diabetes: correlations with diabetic duration and functional impairments. *Brain : a journal of neurology*. Jul 2004;127(Pt 7):1593-605. doi:10.1093/brain/awh180
52. Loseth S, Stalberg E, Jorde R, Mellgren SI. Early diabetic neuropathy: thermal thresholds and intraepidermal nerve fibre density in patients with normal nerve conduction studies. *Journal of neurology*. Aug 2008;255(8):1197-202. doi:10.1007/s00415-008-0872-0
53. Quattrini C, Tavakoli M, Jeziorska M, et al. Surrogate markers of small fiber damage in human diabetic neuropathy. *Diabetes*. Aug 2007;56(8):2148-54. doi:10.2337/db07-0285
54. Sorensen L, Molyneaux L, Yue DK. The relationship among pain, sensory loss, and small nerve fibers in diabetes. *Diabetes care*. Apr 2006;29(4):883-7. doi:10.2337/diacare.29.04.06.dc05-2180
55. Smith AG, Russell J, Feldman EL, et al. Lifestyle intervention for pre-diabetic neuropathy. *Diabetes care*. Jun 2006;29(6):1294-9. doi:10.2337/dc06-0224
56. Garber AJ, Handelsman Y, Grunberger G, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm - 2020 Executive Summary. *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*. Jan 2020;26(1):107-139. doi:10.4158/CS-2019-0472
57. Vinik AI, Camacho PM, Davidson JA, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Position Statement on Testing for Autonomic and Somatic Nerve Dysfunction *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*. Dec 2017;23(12):1472-1478. doi:10.4158/ep-2017-0053
58. Cruccu G, Sommer C, Anand P, et al. EFNS guidelines on neuropathic pain assessment: revised 2009. *Eur J Neurol*. Aug 2010;17(8):1010-8. doi:10.1111/j.1468-1331.2010.02969.x
59. Pop-Busui R, Boulton AJ, Feldman EL, et al. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. *Diabetes care*. Jan 2017;40(1):136-154. doi:10.2337/dc16-2042
60. ADA. 10. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes—2018. 10.2337/dc18-S010. *Diabetes care*. 2018;41(Supplement 1):S105.
61. ADA. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. *Diabetes care*. Jan 2020;43(Suppl 1):S14-s31. doi:10.2337/dc20-S002

62. ADA. Standards of Medical Care in Diabetes—2021 Abridged for Primary Care Providers. *Clinical Diabetes*. 2021;39(1):14-43. doi:10.2337/cd21-as01
63. ADA. Standards of Medical Care in Diabetes—2022 Abridged for Primary Care Providers. *Clinical Diabetes*. 2022;40(1):10-38. doi:10.2337/cd22-as01
64. ADA. Standards of Care in Diabetes-2023 Abridged for Primary Care Providers. *Clin Diabetes*. Winter 2023;41(1):4-31. doi:10.2337/cd23-as01
65. ADA. 12. Retinopathy, Neuropathy, and Foot Care: Standards of Care in Diabetes—2025. *Diabetes care*. 2025;48(Supplement_1):S252-S265. doi:doi.org/10.2337/dc25-S012
66. ADA. Standards of Medical Care in Diabetes—2019 Abridged for Primary Care Providers. *Clinical Diabetes*. 2019;37(1):11-34. doi:10.2337/cd18-0105
67. Burlina AP, Sims KB, Politei JM, et al. Early diagnosis of peripheral nervous system involvement in Fabry disease and treatment of neuropathic pain: the report of an expert panel. *BMC Neurol*. 2011;11:61. doi:10.1186/1471-2377-11-61
68. Smith SM, Dworkin RH, Turk DC, et al. The potential role of sensory testing, skin biopsy, and functional brain imaging as biomarkers in chronic pain clinical trials: IMMPACT considerations. *J Pain*. Jul 2017;18(7):757-77. doi:10.1016/j.jpain.2017.02.429
69. Haanpaa M, Attal N, Backonja M, et al. NeuPSIG guidelines on neuropathic pain assessment. *Pain*. Jan 2011;152(1):14-27. doi:10.1016/j.pain.2010.07.031

Policy Update History:

Approval Date	Effective Date; Summary of Changes
01/12/2026	05/01/2026; Document updated with literature review. Reimbursement Information unchanged. References revised.
10/30/2024	01/15/2025: Document updated with literature review. Reimbursement Information unchanged. References revised.
03/01/2024	03/01/2024: Document updated with literature review. Reimbursement Information revised for clarity. Added code 88313; removed codes 88305, 88314. References revised.
11/01/2023	11/01/2023: Document updated with literature review. Reimbursement information revised for clarity; no additional information added. References revised.
11/1/2022	11/01/2022: New policy