



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 New Mexico may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSNM 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.

## **Serum Biomarker Testing for Multiple Sclerosis and Related Neurologic Diseases**

**Policy Number: CPCPLAB036**

**Version 1.0**

**Approval Date: Nov. 19, 2024**

**Plan Effective Date: January 15, 2025**

## Description

BCBSNM 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 multiple sclerosis (MS), cerebrospinal fluid (CSF) and serum oligoclonal band analysis **may be reimbursable** in any of the following situations:
  - a. For individuals with atypical clinical, laboratory, or imaging features;
  - b. For individuals with an atypical clinically isolated syndrome including, but not limited to, primary progressive multiple sclerosis or relapsing-remitting course;
  - c. For individuals belonging to a population in which MS is less common (e.g., children, older individuals);
  - d. For individuals with insufficient clinical or imaging evidence for diagnosis.
2. In cases of suspected neuromyelitis optica spectrum disorders (NMOSD) or myelin oligodendrocyte glycoprotein-immunoglobulin G (MOG-IgG)-associated encephalomyelitis (MOG-EM), serum indirect fluorescence assay or fluorescence-activated cell sorting (FACS) assay of aquaporin-4-IgG (AQP4-IgG) and MOG-IgG **may be reimbursable** when **all** the following conditions are met:
  - a. The individual has monophasic or relapsing acute optic neuritis, myelitis, brainstem encephalitis, encephalitis, or any combination thereof;
  - b. The individual has radiological or electrophysiological findings compatible with central nervous system (CNS) demyelination;
  - c. The individual has at least one of the following:
    - i. Belongs to a higher risk population (e.g., pediatric);
    - ii. Has an abnormal MRI depicting extensive optic nerve lesion, extensive spinal cord lesion or atrophy, or large confluent T2 brain lesions;
    - iii. Has prominent papilledema/papillitis/optic disc swelling during acute optic neuritis;
    - iv. Has neutrophilic CSF pleocytosis; OR
    - v. Has a histopathology finding of primary demyelination with intraleisional complement and IgG deposits or has a previous diagnosis of "pattern II MS";
    - vi. Has simultaneous bilateral acute optic neuritis;
    - vii. Has a severe visual deficit or blindness in one or both eyes during or after acute optic neuritis;
    - viii. Has severe or frequent episodes of acute myelitis or brainstem encephalitis;
    - ix. Has permanent sphincter and/or erectile disorder after myelitis;

- x. Has a previous diagnosis of acute disseminated encephalomyelitis (ADEM).
3. In all other situations, serum biomarker tests for multiple sclerosis **are not reimbursable**.
  4. ELISA, Western blot, immunohistochemistry, or any other serum assays to test for NMOSD or MOG-EM **are not reimbursable**.
  5. For the diagnosis of MS, NMOSD, or MOG-EM, all other cerebrospinal fluid (CSF) biomarker tests, including AQP4-IgG or MOG-IgG **are not reimbursable**.

## Procedure Codes

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

<b>Codes</b>
83520, 83884, 83916, 84182, 86051, 86052, 86053, 86362, 86363, 88341, 88342, 0443U

## References:

- Atlas of MS. (2023). *MS Statistics*. <https://www.atlasofms.org/map/united-states-of-america/epidemiology/number-of-people-with-ms>
- Benkert, P., Meier, S., Schaedelin, S., Manouchehrinia, A., Yaldizli, Ö., Maceski, A., Oechtering, J., Achtnichts, L., Conen, D., Derfuss, T., Lalive, P. H., Mueller, C., Müller, S., Naegelin, Y., Oksenberg, J. R., Pot, C., Salmen, A., Willemse, E., Kockum, I., . . . Kuhle, J. (2022). Serum neurofilament light chain for individual prognostication of disease activity in people with multiple sclerosis: a retrospective modelling and validation study. *Lancet Neurol*, 21(3), 246-257. [https://doi.org/10.1016/s1474-4422\(22\)00009-6](https://doi.org/10.1016/s1474-4422(22)00009-6)
- Brownlee, W. J., Hardy, T. A., Fazekas, F., & Miller, D. H. (2017). Diagnosis of multiple sclerosis: progress and challenges. *Lancet*, 389(10076), 1336-1346. [https://doi.org/10.1016/s0140-6736\(16\)30959-x](https://doi.org/10.1016/s0140-6736(16)30959-x)
- Cantó, E., Barro, C., Zhao, C., Caillier, S. J., Michalak, Z., Bove, R., Tomic, D., Santaniello, A., Häring, D. A., Hollenbach, J., Henry, R. G., Cree, B. A. C., Kappos, L., Leppert, D., Hauser, S. L., Benkert, P., Oksenberg, J. R., & Kuhle, J. (2019). Association Between Serum Neurofilament Light Chain Levels and Long-term Disease Course Among Patients With Multiple Sclerosis Followed up for 12 Years. *JAMA Neurol*, 76(11), 1359-1366. <https://doi.org/10.1001/jamaneurol.2019.2137>
- Comabella, M., & Montalban, X. (2014). Body fluid biomarkers in multiple sclerosis. *Lancet Neurol*, 13(1), 113-126. [https://doi.org/10.1016/s1474-4422\(13\)70233-3](https://doi.org/10.1016/s1474-4422(13)70233-3)
- Comabella, M., Sastre-Garriga, J., & Montalban, X. (2016). Precision medicine in multiple sclerosis: biomarkers for diagnosis, prognosis, and treatment response. *Curr Opin Neurol*, 29(3), 254-262. <https://doi.org/10.1097/wco.0000000000000336>

- El Ayoubi, N. K., & Khouri, S. J. (2017). Blood Biomarkers as Outcome Measures in Inflammatory Neurologic Diseases. *Neurotherapeutics*, 14(1), 135-147.  
<https://doi.org/10.1007/s13311-016-0486-7>
- Eriksson, M., Andersen, O., & Runmarker, B. (2003). Long-term follow up of patients with clinically isolated syndromes, relapsing-remitting and secondary progressive multiple sclerosis. *Mult Scler*, 9(3), 260-274.  
<https://doi.org/10.1191/1352458503ms914oa>
- FDA. (2016). 510k. [https://www.accessdata.fda.gov/cdrh\\_docs/pdf16/K161951.pdf](https://www.accessdata.fda.gov/cdrh_docs/pdf16/K161951.pdf)
- Filippi, M., & Rocca, M. A. (2011). MR imaging of multiple sclerosis. *Radiology*, 259(3), 659-681. <https://doi.org/10.1148/radiol.11101362>
- Fryer, J. P., Lennon, V. A., Pittock, S. J., Jenkins, S. M., Fallier-Becker, P., Clardy, S. L., Horta, E., Jedynak, E. A., Lucchinetti, C. F., Shuster, E. A., Weinshenker, B. G., Wingerchuk, D. M., & McKeon, A. (2014). AQP4 autoantibody assay performance in clinical laboratory service. *Neurol Neuroimmunol Neuroinflamm*, 1(1), e11.  
<https://doi.org/10.1212/NXI.00000000000000011>
- Gil-Perotin, S., Castillo-Villalba, J., Cubas-Nuñez, L., Gasque, R., Hervas, D., Gomez-Mateu, J., Alcala, C., Perez-Miralles, F., Gascon, F., Dominguez, J. A., & Casanova, B. (2019). Combined Cerebrospinal Fluid Neurofilament Light Chain Protein and Chitinase-3 Like-1 Levels in Defining Disease Course and Prognosis in Multiple Sclerosis. *Front Neurol*, 10, 1008. <https://doi.org/10.3389/fneur.2019.01008>
- Glisson, C. C. (2024). *Neuromyelitis optica spectrum disorders*. Wolters Kluwer.  
<https://www.uptodate.com/contents/neuromyelitis-optica-spectrum-disorders-nmosd-clinical-features-and-diagnosis>
- Goodin, D. S. (2014). The epidemiology of multiple sclerosis: insights to disease pathogenesis. *Handb Clin Neurol*, 122, 231-266. <https://doi.org/10.1016/b978-0-444-52001-2.00010-8>
- Hyun, J. W., Kim, W., Huh, S. Y., Park, M. S., Ahn, S. W., Cho, J. Y., Kim, B. J., Lee, S. H., Kim, S. H., & Kim, H. J. (2018). Application of the 2017 McDonald diagnostic criteria for multiple sclerosis in Korean patients with clinically isolated syndrome. *Mult Scler*, 1352458518790702. <https://doi.org/10.1177/1352458518790702>
- Jarius, S., Paul, F., Aktas, O., Asgari, N., Dale, R. C., de Seze, J., Franciotta, D., Fujihara, K., Jacob, A., Kim, H. J., Kleiter, I., Kümpfel, T., Levy, M., Palace, J., Ruprecht, K., Saiz, A., Trebst, C., Weinshenker, B. G., & Wildemann, B. (2018). MOG encephalomyelitis: international recommendations on diagnosis and antibody testing. *Journal of Neuroinflammation*, 15, 134. <https://doi.org/10.1186/s12974-018-1144-2>
- Jitprapaikulsan, J., Chen, J. J., Flanagan, E. P., Tobin, W. O., Fryer, J. P., Weinshenker, B. G., McKeon, A., Lennon, V. A., Leavitt, J. A., Tillema, J. M., Lucchinetti, C., Keegan, B. M., Kantarci, O., Khanna, C., Jenkins, S. M., Spears, G. M., Sagan, J., & Pittock, S. J. (2018). Aquaporin-4 and Myelin Oligodendrocyte Glycoprotein Autoantibody Status Predict Outcome of Recurrent Optic Neuritis. *Ophthalmology*, 125(10), 1628-1637. <https://doi.org/10.1016/j.ophtha.2018.03.041>
- Koch, M., Kingwell, E., Rieckmann, P., & Tremlett, H. (2009). The natural history of primary progressive multiple sclerosis. *Neurology*, 73(23), 1996-2002.  
<https://doi.org/10.1212/WNL.0b013e3181c5b47f>
- Lim, C. K., Bilgin, A., Lovejoy, D. B., Tan, V., Bustamante, S., Taylor, B. V., Bessede, A., Brew, B. J., & Guillemain, G. J. (2017). Kynurenone pathway metabolomics predicts

- and provides mechanistic insight into multiple sclerosis progression. *Sci Rep*, 7, 41473. <https://doi.org/10.1038/srep41473>
- Lotze, T. E. (2024). *Differential diagnosis of acute central nervous system demyelination in children*. Wolters Kluwer. <https://www.uptodate.com/contents/differential-diagnosis-of-acute-central-nervous-system-demyelination-in-children>
- Lublin, F. D., Coetzee, T., Cohen, J. A., Marrie, R. A., Thompson, A. J., & International Advisory Committee on Clinical Trials in, M. S. (2020). The 2013 clinical course descriptors for multiple sclerosis: A clarification. *Neurology*, 94(24), 1088-1092. <https://doi.org/10.1212/WNL.00000000000009636>
- Lublin, F. D., Reingold, S. C., Cohen, J. A., Cutter, G. R., Sorensen, P. S., Thompson, A. J., Wolinsky, J. S., Balcer, L. J., Banwell, B., Barkhof, F., Bebo, B., Jr., Calabresi, P. A., Clanet, M., Comi, G., Fox, R. J., Freedman, M. S., Goodman, A. D., Inglesi, M., Kappos, L., . . . Polman, C. H. (2014). Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*, 83(3), 278-286. <https://doi.org/10.1212/wnl.0000000000000560>
- Luzzio, C. (2023). Multiple Sclerosis Guidelines. <https://emedicine.medscape.com/article/1146199-guidelines>
- Martin, S.-J., McGlasson, S., Hunt, D., & Overell, J. (2019). Cerebrospinal fluid neurofilament light chain in multiple sclerosis and its subtypes: a meta-analysis of case-control studies. *Journal of Neurology, Neurosurgery & Psychiatry*, 90(9), 1059. <https://doi.org/10.1136/jnnp-2018-319190>
- NICE. (2022). Multiple sclerosis in adults: management. <https://www.nice.org.uk/guidance/ng220/chapter/Recommendations#diagnosing-multiple-sclerosis>
- Offenbacher, H., Fazekas, F., Schmidt, R., Freidl, W., Flooh, E., Payer, F., & Lechner, H. (1993). Assessment of MRI criteria for a diagnosis of MS. *Neurology*, 43(5), 905-909. <https://doi.org/10.1212/wnl.43.5.905>
- Olek, M., Howard, Jonathan. (2024a). Clinical course and classification of multiple sclerosis - UpToDate. In J. Dashe (Ed.), *UpToDate*. <https://www.uptodate.com/contents/clinical-presentation-course-and-prognosis-of-multiple-sclerosis-in-adults>
- Olek, M., Howard, Jonathan. (2024b). Evaluation and diagnosis of multiple sclerosis in adults. In J. Dashe (Ed.), *UpToDate*. <https://www.uptodate.com/contents/evaluation-and-diagnosis-of-multiple-sclerosis-in-adults>
- Raphael, I., Webb, J., Stuve, O., Haskins, W. E., & Forsthuber, T. G. (2015). Body fluid biomarkers in multiple sclerosis: how far we have come and how they could affect the clinic now and in the future. *Expert Rev Clin Immunol*, 11(1), 69-91. <https://doi.org/10.1586/1744666x.2015.991315>
- Rovira, A., Swanton, J., Tintore, M., Huerga, E., Barkhof, F., Filippi, M., Frederiksen, J. L., Langkilde, A., Miszkiel, K., Polman, C., Rovaris, M., Sastre-Garriga, J., Miller, D., & Montalban, X. (2009). A single, early magnetic resonance imaging study in the diagnosis of multiple sclerosis. *Arch Neurol*, 66(5), 587-592. <https://doi.org/10.1001/archneurol.2009.49>
- Sapko, K., Jamroz-Wisniewska, A., Marciniec, M., Kulczynski, M., Szczepanska-Szerej, A., & Rejdak, K. (2020). Biomarkers in Multiple Sclerosis: a review of diagnostic and prognostic factors. *Neurol Neurochir Pol*, 54(3), 252-258. <https://doi.org/10.5603/PJNNS.a2020.0037>

- Schaffler, N., Kopke, S., Winkler, L., Schippling, S., Inglese, M., Fischer, K., & Heesen, C. (2011). Accuracy of diagnostic tests in multiple sclerosis--a systematic review. *Acta Neurol Scand*, 124(3), 151-164. <https://doi.org/10.1111/j.1600-0404.2010.01454.x>
- Simonsen, C. S., Flemmen, H., Lauritzen, T., Berg-Hansen, P., Moen, S. M., & Celius, E. G. (2020). The diagnostic value of IgG index versus oligoclonal bands in cerebrospinal fluid of patients with multiple sclerosis. *Mult Scler J Exp Transl Clin*, 6(1), 2055217319901291. <https://doi.org/10.1177/2055217319901291>
- Sotirchos, E. S., Filippatou, A., Fitzgerald, K. C., Salama, S., Pardo, S., Wang, J., Ogbuokiri, E., Cowley, N. J., Pellegrini, N., Murphy, O. C., Mealy, M. A., Prince, J. L., Levy, M., Calabresi, P. A., & Saidha, S. (2019). Aquaporin-4 IgG seropositivity is associated with worse visual outcomes after optic neuritis than MOG-IgG seropositivity and multiple sclerosis, independent of macular ganglion cell layer thinning. *Mult Scler*, 1352458519864928. <https://doi.org/10.1177/1352458519864928>
- Teunissen, C. E., Malekzadeh, A., Leurs, C., Bridel, C., & Killestein, J. (2015). Body fluid biomarkers for multiple sclerosis--the long road to clinical application. *Nat Rev Neurol*, 11(10), 585-596. <https://doi.org/10.1038/nrneurol.2015.173>
- Thompson, A. J., Banwell, B. L., Barkhof, F., Carroll, W. M., Coetzee, T., Comi, G., Correale, J., Fazekas, F., Filippi, M., Freedman, M. S., Fujihara, K., Galetta, S. L., Hartung, H. P., Kappos, L., Lublin, F. D., Marrie, R. A., Miller, A. E., Miller, D. H., Montalban, X., . . . Cohen, J. A. (2018). Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*, 17(2), 162-173. [https://doi.org/10.1016/s1474-4422\(17\)30470-2](https://doi.org/10.1016/s1474-4422(17)30470-2)
- Wallin, M. T., Culpepper, W. J., Campbell, J. D., Nelson, L. M., Langer-Gould, A., Marrie, R. A., Cutter, G. R., Kaye, W. E., Wagner, L., Tremlett, H., Buka, S. L., Dilokthornsakul, P., Topol, B., Chen, L. H., & LaRocca, N. G. (2019). The prevalence of MS in the United States: A population-based estimate using health claims data. *Neurology*, 92(10), e1029-e1040. <https://doi.org/10.1212/wnl.0000000000007035>
- Weinshenker, B. G. (1994). Natural history of multiple sclerosis. *Ann Neurol*, 36 Suppl, S6-11. <https://doi.org/10.1002/ana.410360704>
- Wingerchuk, D. M., Banwell, B., Bennett, J. L., Cabre, P., Carroll, W., Chitnis, T., de Seze, J., Fujihara, K., Greenberg, B., Jacob, A., Jarius, S., Lana-Peixoto, M., Levy, M., Simon, J. H., Tenembaum, S., Traboulsee, A. L., Waters, P., Wellik, K. E., & Weinshenker, B. G. (2015). International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology*, 85(2), 177-189. <https://doi.org/10.1212/wnl.0000000000001729>
- Yang, J., Hamade, M., Wu, Q., Wang, Q., Axtell, R., Giri, S., & Mao-Draayer, Y. (2022). Current and Future Biomarkers in Multiple Sclerosis. *Int J Mol Sci*, 23(11). <https://doi.org/10.3390/ijms23115877>

## Policy Update History:

<b>Approval Date</b>	<b>Effective Date; Summary of Changes</b>
11/19/2024	01/15/2025: Added new CPT code 83884 effective 01/01/2025.
10/30/2024	01/15/2025; Document updated with literature review. Reimbursement Information unchanged. Added code 0443U. References revised; some updated; no new references added.
02/01/2024	02/01/2024: Document updated with literature review. The following changes were made to Reimbursement Information: removed ethnicity from 1c and 2c. References revised.
11/01/2023	11/01/2023: Document updated with literature review. The following changes were made to the Reimbursement Information section: #2 revised to indicate the services may be reimbursable when all of the criteria listed are met. Other changes made for clarity. References revised.
11/1/2022	11/01/2022: New policy