



If a conflict arises between a Clinical Payment and Coding Policy (“CPCP”) 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. BCBSNM 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 (“HIPAA”) approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing (“UB”) Editor, American Medical Association (“AMA”), Current Procedural Terminology (“CPT®”), CPT® Assistant, Healthcare Common Procedure Coding System (“HCPCS”), ICD-10 CM and PCS, National Drug Codes (“NDC”), Diagnosis Related Group (“DRG”) guidelines, Centers for Medicare and Medicaid Services (“CMS”) National Correct Coding Initiative (“NCCI”) 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

Plan CMO Approval Date: July 27, 2022

Plan Effective Date: January 1, 2023

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. Cerebrospinal fluid (CSF) and serum oligoclonal band analysis **may be reimbursable** for multiple sclerosis in any of the following situations:
 - a. Atypical clinical, laboratory, or imaging features; OR

- b. An atypical clinically isolated syndrome such as but not limited to, primary progressive multiple sclerosis or relapsing-remitting course; OR
 - c. Belongs to a population in which MS is less common, such as but not limited to, children, older individuals, or non-Caucasians; OR
 - d. Insufficient clinical or imaging evidence for diagnosis.
2. Serum indirect fluorescence assay or fluorescence-activated cell sorting (FACS) assay of aquaporin-4-IgG (AQP4-IgG) and myelin oligodendrocyte glycoprotein (MOG-IgG) in cases of suspected NMOSD, including NMO, or MOG-EM **may be reimbursable** when the following conditions are met:
- a. Monophasic or relapsing acute optic neuritis, myelitis, brainstem encephalitis, encephalitis, or any combination thereof; AND
 - b. Radiological or electrophysiological findings compatible with CNS demyelination; AND
 - c. At least one of the following:
 - i. Belong to a higher risk population—African American, Latin American, Asian, or pediatric; OR
 - ii. Abnormal MRI depicting extensive optic nerve lesion, extensive spinal cord lesion or atrophy, or large confluent T2 brain lesions; OR
 - iii. Prominent papilledema/papillitis/optic disc swelling during acute optic neuritis; OR
 - iv. Neutrophilic CSF pleocytosis; OR
 - v. Histopathology finding primary demyelination with intralesional complement and IgG deposits or previous diagnosis of “pattern II MS”; OR
 - vi. Simultaneous bilateral acute optic neuritis; OR
 - vii. Severe visual deficit or blindness in one or both eyes during or after acute optic neuritis; OR
 - viii. Severe or frequent episodes of acute myelitis or brainstem encephalitis; OR
 - ix. Permanent sphincter and/or erectile disorder after myelitis; OR
 - x. Previous diagnosis of acute disseminated encephalomyelitis (ADEM).
3. Serum biomarker tests for multiple sclerosis **is not reimbursable** in all other situations.
4. ELISA, Western blot, immunohistochemistry, or any other serum assays to test for NMOSD or MOG-EM **is not reimbursable**.
5. All other cerebrospinal fluid (CSF) biomarker tests, including AQP4-IgG or MOG-IgG, for multiple sclerosis, NMOSD, or MOG-EM **is not reimbursable**

Procedure Codes

Codes
83520, 83916, 84182, 86255, 86256, 88341, 88342

References:

Anderson, D. W., Ellenberg, J. H., Leventhal, C. M., Reingold, S. C., Rodriguez, M., & Silberberg, D. H. (1992). Revised estimate of the prevalence of multiple sclerosis in the United States. *Ann Neurol*, 31(3), 333-336. doi:10.1002/ana.410310317

Brownlee, W. J., Hardy, T. A., Fazekas, F., & Miller, D. H. (2017). Diagnosis of multiple sclerosis: progress and challenges. *Lancet*, 389(10076), 1336-1346. doi:10.1016/s0140-6736(16)30959-x

Cantó, E., Barro, C., Zhao, C., Caillier, S. J., Michalak, Z., Bove, 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. doi:10.1001/jamaneurol.2019.2137

Comabella, M., & Montalban, X. (2014). Body fluid biomarkers in multiple sclerosis. *Lancet Neurol*, *13*(1), 113-126. doi: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. doi:10.1097/wco.0000000000000336

Dilokthornsakul, P., Valuck, R. J., Nair, K. V., Corboy, J. R., Allen, R. R., & Campbell, J. D. (2016). Multiple sclerosis prevalence in the United States commercially insured population. *Neurology*, *86*(11), 1014-1021. doi:10.1212/wnl.0000000000002469

El Ayoubi, N. K., & Houry, S. J. (2017). Blood Biomarkers as Outcome Measures in Inflammatory Neurologic Diseases. *Neurotherapeutics*, *14*(1), 135-147. doi: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. doi:10.1191/1352458503ms914oa

FDA. (2016). 510k. Retrieved from https://www.accessdata.fda.gov/cdrh_docs/pdf16/K161951.pdf

FDA. (2021). Devices@FDA. Retrieved from <https://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm>

Filippi, M., & Rocca, M. A. (2011). MR imaging of multiple sclerosis. *Radiology*, *259*(3), 659-681. doi:10.1148/radiol.11101362

Fryer, J. P., Lennon, V. A., Pittock, S. J., Jenkins, S. M., Fallier-Becker, P., Clardy, S. L., . . . McKeon, A. (2014). AQP4 autoantibody assay performance in clinical laboratory service. *Neurol Neuroimmunol Neuroinflamm*, *1*(1), e11. doi:10.1212/nxi.0000000000000011

Gil-Perotin, S., Castillo-Villalba, J., Cubas-Nuñez, L., Gasque, R., Hervas, D., Gomez-Mateu, J., . . . 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. doi:10.3389/fneur.2019.01008

Glisson, C. C. (2019). Neuromyelitis optica spectrum disorders. *UpToDate*. Retrieved from <https://www.uptodate.com/contents/neuromyelitis-optica-spectrum-disorders>

Goodin, D. S. (2014). The epidemiology of multiple sclerosis: insights to disease pathogenesis. *Handb Clin Neurol*, *122*, 231-266. doi: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, H. J. (2018). Application of the 2017 McDonald diagnostic criteria for multiple sclerosis in Korean patients with clinically isolated syndrome. *Mult Scler*, 1352458518790702. doi:10.1177/1352458518790702

Jarius, S., Paul, F., Aktas, O., Asgari, N., Dale, R. C., de Seze, J., . . . Wildemann, B. (2018). MOG encephalomyelitis: international recommendations on diagnosis and antibody testing. *Journal of Neuroinflammation*, *15*, 134. doi:10.1186/s12974-018-1144-2

Jitrapaikulsan, J., Chen, J. J., Flanagan, E. P., Tobin, W. O., Fryer, J. P., Weinshenker, B. G., . . . Pittock, S. J. (2018). Aquaporin-4 and Myelin Oligodendrocyte Glycoprotein Autoantibody Status Predict Outcome of Recurrent Optic Neuritis. *Ophthalmology*, *125*(10), 1628-1637. doi: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. doi:10.1212/WNL.0b013e3181c5b47f

Lim, C. K., Bilgin, A., Lovejoy, D. B., Tan, V., Bustamante, S., Taylor, B. V., . . . Guillemin, G. J. (2017). Kynurenine pathway metabolomics predicts and provides mechanistic insight into multiple sclerosis progression. *Sci Rep*, *7*, 41473. doi:10.1038/srep41473

Lotze, T. E. (2019). Differential diagnosis of acute central nervous system demyelination in children. *UpToDate*. Retrieved from <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. doi:10.1212/WNL.0000000000009636

Lublin, F. D., & Reingold, S. C. (1996). Defining the clinical course of multiple sclerosis: results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis. *Neurology*, *46*(4), 907-911. Retrieved from <http://dx.doi.org/>

Lublin, F. D., Reingold, S. C., Cohen, J. A., Cutter, G. R., Sorensen, P. S., Thompson, A. J., . . . Polman, C. H. (2014). Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*, *83*(3), 278-286. doi:10.1212/wnl.0000000000000560

Luzzio, C. (2019). Multiple Sclerosis Guidelines. Retrieved from <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. doi:10.1136/jnnp-2018-319190

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. Retrieved from <http://dx.doi.org/>

Olek, M. (2019). Clinical course and classification of multiple sclerosis - UpToDate. In J. Dashe (Ed.), *UpToDate*. Retrieved from https://www.uptodate.com/contents/clinical-course-and-classification-of-multiple-sclerosis?source=see_link

Olek, M., Howard, Jonathan. (2019). Evaluation and diagnosis of multiple sclerosis in adults. In J. Dashe (Ed.), *UpToDate*. Retrieved from <https://www.uptodate.com/contents/evaluation-and-diagnosis-of-multiple-sclerosis-in->

adults?search=multiple%20sclerosis&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H11

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. doi:10.1586/1744666x.2015.991315

Rovira, A., Swanton, J., Tintore, M., Huerga, E., Barkhof, F., Filippi, M., . . . Montalban, X. (2009). A single, early magnetic resonance imaging study in the diagnosis of multiple sclerosis. *Arch Neurol*, *66*(5), 587-592. doi:10.1001/archneurol.2009.49

Sapko, K., Jamroz-Wisniewska, A., Marciniak, 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. doi: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. doi: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. doi:10.1177/2055217319901291

Sotirchos, E. S., Filippatou, A., Fitzgerald, K. C., Salama, S., Pardo, S., Wang, J., . . . 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. doi: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. doi:10.1038/nrneurol.2015.173

Thompson, A. J., Banwell, B. L., Barkhof, F., Carroll, W. M., Coetzee, T., Comi, G., . . . Cohen, J. A. (2018). Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*, *17*(2), 162-173. doi:10.1016/s1474-4422(17)30470-2

Weinshenker, B. G. (1994). Natural history of multiple sclerosis. *Ann Neurol*, *36* Suppl, S6-11. Retrieved from <http://dx.doi.org/>

Wingerchuk, D. M., Banwell, B., Bennett, J. L., Cabre, P., Carroll, W., Chitnis, T., . . . Weinshenker, B. G. (2015). International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology*, *85*(2), 177-189. doi:10.1212/wnl.0000000000001729

Policy Update History:

1/1/2023	New policy
----------	------------