KAISER PERMANENTE®

Kaiser Foundation Health Plan of Washington

Clinical Review Criteria

Serum Biomarker Tests for Multiple Sclerosis

- gMS®Dx Testing
- gMS®Pro EDSS Testing

Criteria

For Medicare Members

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	Cytogenetic Studies (190.3)
Local Coverage Determinations (LCD)	None
Local Coverage Article	None

For Non-Medicare Members

There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.

If requesting this service, please send the following documentation to support medical necessity:

- Last 6 months of clinical notes from requesting provider &/or specialist

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background

Multiple sclerosis (MS) is a chronic illness of the central nervous system. Diagnosis of MS can be very difficult as there are no clinical findings that are unique to MS. The revised McDonald's Criteria, which incorporated clinical, radiologic, and laboratory findings are often used to diagnose MS. However, because the use of these criteria frequently results in delayed diagnosis, researchers have been trying to find reliable biomarkers that would help to establish a diagnosis (Harris 2009).

The **gMS®Dx test**, a new blood-based test for MS biomarkers, was developed by Glycominds to help physicians identify patients with a high probability of developing MS. The biomarker used in the gMS®Dx test is based on IgM antibodies against the a-glucose antigen (GAGA4). The test is designed to be used in patients as a part of the MS diagnostic work-up and is recommended for use in suspected MS patients for which the diagnosis of MS has not yet been confirmed. The results of the test are reported as negative (patient may still have MS or other neurological disease, continue with routine testing), positive (patient has a high likelihood of having MS), high positive (patient has a very high likelihood of having MS) (Glycominds 2012). One advantage of the gMS®Dx test is that blood samples are relatively easy to obtain and are minimally invasive. A limitation of using biomarkers for diagnosing MS is that they may be affected by other systematic events such as viral infections (Harris 2009). An additional limitation of the gMS®Dx test is that the biologic basis for the MS biomarker is unclear (Freeman 2009).

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Multiple sclerosis (MS) is a complex disease with heterogeneous clinical presentation and disease course. Because prognosis is so hard to predict there has been interest in indentifying biomarkers that are associated with disease progression (Harris 2009).

Glycominds has developed the **gMS®Pro EDSS test**, a blood-based test that uses biomarkers to identify patients at high risk for severe disease progression. The biomarkers used in the gMS®Pro EDSS test are based on IgM antibodies against the a-glucose antigen (GAGA2, GAGA3, GAGA4, GAGA6). The aim of this test is to help clinicians choose the most appropriate disease treatment. The test is designed for use in patients at their first episode and for patients with relapse-remitting multiple sclerosis during their first decade of the disease. The results of the test are reported as negative (patient has a low risk to fast disability progression as measured by EDSS) or positive (patient has a high risk to fast disability progression as measured by EDSS) (Glycominds 2012). One advantage of the gMS®Pro EDSS test is that blood samples are relatively easy to obtain and are minimally invasive. A limitation of using biomarkers for diagnosing MS is that biomarkers may be affected by other systematic events such as viral infections (Harris 2009). An additional limitation of the gMS®Pro EDSS test is that the biologic basis for the MS biomarkers is unclear (Freeman 2009).

Medical Technology Assessment Committee (MTAC)

gMS®Dx and gMS®Pro EDSS

06/18/2012: MTAC REVIEW

Evidence Conclusion: Diagnostic accuracy**:** Results from a recent observational study with several limitations suggest that the gMS®Dx test has a sensitivity or 33.7% (95% CI, 30.2 to 37.3) and a specificity of 98.5% (95% CI, 91.7 to 100) for differentiating relapsing remitting multiple sclerosis (RRMS)/secondary progressive multiple sclerosis (SPMS) from other neurological disorders (Brettschneider 2009). Impact on diagnosis: There is insufficient evidence to determine whether the gMS®Dx test will impact diagnosis. Impact on patient management: There is insufficient evidence to determine whether the gMS®Dx test will change patient's management. Conclusion: Diagnostic accuracy: Weak evidence suggest that the gMS®Dx test has a sensitivity or 33.7% and a specificity of 98.5% for differentiating RRMS/SPMS from other neurological disorders. Impact on diagnosis: There is insufficient evidence to determine whether the gMS®Dx test will impact diagnosis. Impact on patient management: There is insufficient evidence to determine whether the gMS®Dx test will change patient's management.

gMS®Pro EDSS testing

06/18/2012: MTAC REVIEW

Evidence Conclusion: Accuracy: A prospective cohort study that included 286 patients with clinically isolated syndrome (CIS) evaluated the prognostic value of the gMS®Pro EDSS test. Results from this study suggest that that the gMS®Pro EDSS test does not significantly predict prognosis, conversion to McDonald MS, or EDSS progression in patients with CIS. Results from this study should be interpreted with caution as this is an exploratory analysis (Freedman 2011). Results from a retrospective study of 100 RRMS patients taken at their first presentation of RRMS suggest that using a panel of 4 different antibodies had a sensitivity of 37.9% and a specificity of 83.3% for predicting early relapse in patients with RRMS following their first presentation. Results from this study should be interpreted with caution as this is a retrospective exploratory analysis (Freedman 2009). Impact on patient management: No studies were identified that address the impact of gMS®Pro EDSS on patient's management. Conclusion: Accuracy: There is insufficient evidence to determine the accuracy of the gMS®Pro EDSS test. Impact on patient management: There is insufficient evidence to determine whether the gMS®Pro EDSS test will change patient's management.

Articles: gMS®Dx test: Several observational studies were identified that addressed the diagnostic accuracy of the gMS®Dx test. The largest study was selected for review. No studies were identified that addressed the impact of the test on diagnosis or patient's management. The following study was selected for review: Brettschneider J, Jaskowski TD, Tumani H, et al. Serum anti-GAGA4 IgM antibodies differentiate relapsing remitting and secondary progressive multiple sclerosis from primary progressive multiple sclerosis and other neurological diseases. J Neuroimmunol. 2009; 217:95-101. **gMS®Pro EDSS test**: Two studies were identified that addressed the accuracy of the gMS®Pro EDSS test. No studies were identified that addressed the clinical utility of the gMS®Pro EDSS test. The following study was selected for review: Freedman M, Metzig C, Kappos L, et al. Predictive nature of IgM anti-alpha-glucose serum biomarker for relapse activity and EDSS progression in CIS patients: a BENEFIT study analysis. Mult Scler. 2011. [Epub ahead of print] See Evidence Table. Freedman MS, Laks J, Dotan N, Altstock RT, Dukler A, Sindic CJ. Anti-alpha-glucose-based glycan IgM antibodies predict relapse activity in multiple sclerosis after the first neurological event. Mult Scler. 2009; 15:422-430. See Evidence Table.

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The use of gMS®Dx and gMS®Pro EDSS testing does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Applicable Codes

Considered Not Medically Necessary:

CPT® or HCPC Codes	Description
No specific codes for this service. Often submitted with unlisted code 84999.	

***Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

****To verify authorization requirements for a specific code by plan type, please use the **Pre-authorization Code Check**.

Date Created	Date Reviewed	Date Last Revised
07/03/2012	07/03/2012[MDCRPC], 05/07/2013[MDCRPC], 3/04/2014[MDCRPC], 01/06/2015[MPC], 09/06/2016[MPC], 07/11/2017[MPC], 06/05/2018[MPC], 06/04/2019[MPC], 06/02/2020[MPC], 06/01/2021[MPC], 06/07/2022[MPC], 06/06/2023[MPC]	07/03/2012

[MDCRPC] Medical Director Clinical Review and Policy Committee
[MPC] Medical Policy Committee

Revision History	Description

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