Medical Policy
Serum Biomarker Tests for Multiple Sclerosis

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Policy Number: 676
BCBSA Reference Number: 2.04.118
NCD/LCD: NA

Related Policies
None

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity
Medicare HMO BlueSM and Medicare PPO BlueSM Members

Serum biomarker tests for multiple sclerosis are INVESTIGATIONAL in all situations.

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products.
See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Outpatient</th>
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<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
<td>This is not a covered service.</td>
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<tr>
<td>Commercial PPO and Indemnity</td>
<td>This is not a covered service.</td>
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<td>Medicare HMO BlueSM</td>
<td>This is not a covered service.</td>
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<td>Medicare PPO BlueSM</td>
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CPT Codes / HCPCS Codes / ICD Codes
Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.
There is no specific CPT code for this test.

**Description**
Serum antibodies to polysaccharide-containing molecules, called glycans, and other potential serum biomarkers are in development for the diagnosis of multiple sclerosis (MS). These tests include gMS® Dx, for patients with a first episode or clinically isolated syndrome (CIS), and the multimarker prognostic test, gMS® Pro EDSS, for predicting deterioration in patients diagnosed with MS.

**Background**

**Disease Description**
Estimated prevalence of MS in North America varies regionally and ranges from 240 of 100,000 in Canada to 191 of 100,000 in Minnesota and 40 of 100,000 in Texas. Women are affected twice as often as men, and median age of onset is 24 years. Most patients (85%) have the relapsing remitting form of MS (RRMS), and of these, 60% to 70% will progress to secondary progressive MS, usually 10 to 30 years after disease onset. Rarer forms are primary progressive MS and progressive relapsing MS.

MS is characterized by destruction of myelin in the central nervous system. Progressive focal demyelination eventually leads to axonal degeneration and cumulative physical and cognitive disabilities. Because any area of the brain, optic nerve, or spinal cord can be affected, symptoms are diverse and may include cognitive, speech, or vision deficits; numbness; pain; weakness or dysooordination; and bowel or bladder dysfunction. Diagnosis is made by clinical symptoms, typical magnetic resonance imaging (MRI) findings, and oligoclonal antibodies in the cerebrospinal fluid according to current McDonald criteria. Diagnosis requires 2 clinical episodes occurring at 2 discreet points in time, or 1 clinical episode (CIS, defined next) with MRI lesions indicating development at 2 discreet points in time (ie, simultaneous appearance of old and new lesions). Disability progression is quantified in practice and in clinical trials by the Kurtzke Expanded Disability Status Scale. Patients with scores less than 5 are fully ambulatory; scores of 5 to 10 are defined by incrementally decreasing ability to walk.

The term clinically isolated syndrome describes patients who have suffered a first episode suggestive of MS but do not meet diagnostic criteria for definite MS. Studies indicated that early treatment with interferon beta-1b (IFNβ-1b) may delay relapse (ie, a second episode), although long-term disability outcomes were unaffected.

In addition to IFNβ-1b, 8 other disease-modifying drugs are currently U.S. Food and Drug Administration (FDA)-approved for first- or second-line treatment of MS with varying degrees of efficacy for reducing relapses and preventing neurological deterioration. First-line treatments include self-injectable drugs (interferon and glatiramer acetate) and newer oral agents, such as fingolimod, teriflunomide, and dimethyl fumarate. Choice of first-line agent depends on severity of initial presentation, patient preference, and adverse effect profile. Patients with more active or refractory disease are more likely to tolerate greater risk for greater efficacy, for example with second- or third-line agents, natalizumab and alemtuzumab.

**Biomarkers**
Glycominds Ltd., based in Israel, markets the diagnostic test, gMS® Dx, for patients with a first episode or CIS, and the multi-marker prognostic test, gMS® Pro EDSS, for predicting deterioration in patients diagnosed with MS. Both tests are based on detection of serum antibodies to glycans, which are polysaccharide- or carbohydrate-containing molecules on the surface of immune and other cells. gMS Dx detects immunoglobulin M (IgM) antibodies to the disaccharide glycan, glucose (α1,4)glucose(α) (GAGA4), and gMS Pro EDSS detects IgM antibodies to GAGA2, -3, -4, and -6. These anti-glycan antibodies are thought to interfere with normal function of the immune system. Temperature controls are implemented during assay runs to prevent IgM precipitation.

Several other serum biomarkers for MS have been investigated, but no other commercially-available tests were identified.
Summary
Multiple sclerosis (MS) is diagnosed according to criteria that incorporate clinical symptoms and magnetic resonance imaging (MRI) and CSF findings. Because 2 clinical episodes are required for diagnosis, diagnosis and treatment may be delayed in patients presenting with a first clinical episode suggestive of MS. Currently, there is no biomarker available to inform diagnosis or prognosis. A serum biomarker is particularly desirable because of ease of repeat measurements.

Antibodies to glycan molecules are thought to impair immune function. Commercial assays are available to measure serum antibody levels to 1 (glucose [α1,4]glucose[α], also called GAGA4) or several (GAGA2, -3, -4, and -6) glycan molecules. These tests, gMS Dx and gMS Pro EDSS, are marketed to aid diagnosis and prognosis in MS, respectively. However, evidence indicates that these tests are in an early stage of development, and both are therefore considered investigational for all uses.

Tests for serum levels of other MS biomarkers currently in development, including but not limited to apoptosis-related molecules, intercellular adhesion molecules, and myelin peptides, are considered investigational.

Policy History

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<tr>
<th>Date</th>
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<tr>
<td>6/2015</td>
<td>New references added from BCBSA National medical policy.</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

References


