***Effective November 1, 2023, refer to CMS Manual 100-02, Chapter 16-General Exclusions from Coverage for services included in this policy.***

BlueCross BlueShield of Alabama

**Name of Blue Advantage Policy:**

# Serum Biomarker Tests for Multiple Sclerosis

Policy #: 563
Latest Review Date: August 2023
Category: Laboratory
**ARCHIVED EFFECTIVE 11/1/2023**

## BACKGROUND:

***Blue Advantage*** *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

**Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare*** *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

## POLICY:

**Blue Advantage** will treat **serum biomarker tests for multiple sclerosis** as a **non-covered benefit** and as **investigational** in all situations.

*Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.*

## DESCRIPTION OF PROCEDURE OR SERVICE:

Multiple sclerosis (MS) an immune-mediated inflammatory demyelinating disease of the central nervous system defined by multifocal areas of demyelination with loss of oligodendrocytes and astroglial scarring. The most common presenting symptoms are sensory disturbances, weakness and visual disturbances. The disease has a highly variable pace and many atypical forms. MS is primarily diagnosed clinically. The core requirement for diagnosis is the demonstration of central nervous system lesion dissemination in time and space, based upon either clinical findings alone or a combination of clinical and MRI findings. The history and physical examination are most important for diagnostic purposes. MRI is the test of choice to support the clinical diagnosis of MS. Prognosis is hard to predict, which has prompted interest in identifying biomarkers that are associated with disease progression.

Several biomarkers have been proposed as useful for MS diagnosis, prognosis, and therapy response prediction that need to be validated in further studies.

Commercially available serum biomarker tests have been proposed as useful for the diagnosis, prognosis prediction, and therapy response prediction of MS. Some examples of commercially available tests for this purpose include:

- gMS® Dx, which is a blood test designed to be used as a companion to magnetic resonance imaging (MRI) in suspected cases of MS at the first neurological event and for individuals with clinically isolated syndrome in order to expedite the diagnosis of relapsing-remitting MS.
- gMS® Pro EDSS, which is designed to be used as a tool to identify individuals with clinically isolated syndrome and relapsing-remitting MS who are at risk for rapid disability progression.

## KEY POINTS:

This policy has been updated with most recent review of literature on August 17, 2023.

**Summary of Evidence**

It has been hypothesized that the diagnosis and prognosis of MS and the monitoring of treatment response and the assessment of the risk of side effects can be facilitated with the help of established biomarkers. Long-term studies of large cohorts are needed to prove the clinical utility of the application of biomarker testing for the diagnosis and prognosis MS. Biomarkers that enable a reliable prediction of the therapy response in order to facilitate individualized therapy are still lacking. Further research is needed using well-designed scientific evidence to validate that the use of biomarkers for MS results in an improvement in net health outcomes.

**Practice Guidelines and Position Statements**

**International Advisory Committee on Clinical Trials in Multiple Sclerosis**

The International Advisory Committee on Clinical Trials in Multiple Sclerosis, jointly sponsored by the US National Multiple Sclerosis Society, the European Committee for Treatment and Research in Multiple Sclerosis, and the Multiple Sclerosis Phenotype Group re-examined multiple sclerosis phenotypes, exploring clinical, imaging, and biomarker advances through working groups and literature searches. They found the following:

The MS Phenotype Group stated that further research is needed to better define the value of imaging and biological markers in assessing, confirming, or revising MS phenotype descriptors. One example of further research needed is as follows: Focused cohort studies in large datasets of clinically well-defined patients of potential fluid-borne (blood, CSF) markers that might allow better definition of clinical phenotypes.

The committee concluded that "To date, there are no clear clinical, imaging, immunologic or pathologic criteria to determine the transition point when relapse remitting MS converts to secondary progressive MS; the transition is usually gradual. This has limited our ability to study the imaging and biomarker characteristics that may distinguish this course.

**The International Panel on Diagnosis of Multiple Sclerosis**

The International Panel on Diagnosis of Multiple Sclerosis reviewed the 2010 McDonald criteria and recommended revisions in 2017. They found the following:

Research to further refine the criteria should focus on optic nerve involvement, validation in diverse populations, and incorporation of advanced imaging, neurophysiological, and body fluid markers.

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

## KEY WORDS:

gMS Dx, gMS Pro EDSS, multiple sclerosis, serum biomarkers

## APPROVED BY GOVERNING BODIES:
FDA-approved tests for serum biomarkers in MS are currently unavailable.

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by CLIA for high-complexity testing. To date, the FDA has chosen not to require any regulatory review of this test.

## BENEFIT APPLICATION:
Coverage is subject to member's specific benefits. Group-specific policy will supersede this policy when applicable.

## CURRENT CODING:
**CPT Codes:**

| | |
|---|---|
| 84999 | Unlisted chemistry procedure |

## REFERENCES:

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## POLICY HISTORY:

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Available for comment September 19 through November 2, 2014
Medical Policy Group, May 2015
Medical Policy Group, August 2016
Medical Policy Group, October 2019
Medical Policy Group, August 2021
Medical Policy Group, October 2021: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
Medical Policy Group, August 2022: Reviewed by consensus. References added. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
Medical Policy Group, August 2023: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
Medical Policy Group, November 2023: Archived effective 11/1/2023.

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