



**MEDICAL COVERAGE POLICY**

**SERVICE: Neutralizing Antibody Testing in Multiple Sclerosis Patients**

<b>Policy Number:</b>	<b>067</b>
<b>Effective Date:</b>	<b>12/01/2019</b>
<b>Last Review:</b>	<b>09/26/2019</b>
<b>Next Review Date:</b>	<b>09/26/2020</b>

**Important note:**

Unless otherwise indicated, this policy will apply to all lines of business. Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

**SERVICE:** Neutralizing Antibody Testing in Multiple Sclerosis Patients

**PRIOR AUTHORIZATION:** Not applicable.

**POLICY:** Testing for neutralizing antibodies against interferon beta is considered not medically necessary. There is insufficient evidence that such testing is clinically useful in guiding the management of members with Multiple Sclerosis (MS).

**OVERVIEW:** Interferon beta is the first-line treatment for relapsing-remitting multiple sclerosis because it has been shown to reduce the frequency and severity of clinical relapses, slow the progression of disability, and suppress signs of disease activity on MRI. But the drug can induce neutralizing antibodies against itself, which may reduce effectiveness. In clinical trials of various interferon beta preparations, the frequencies of neutralizing antibodies varied widely. Subcutaneous administration induced antibodies more frequently than intramuscular administration.

Assays of neutralizing antibodies (NABs) against interferon beta have not been proven to be useful in MS. About 1/3 of individuals develop NABs against interferon beta. Several technologies have been developed to assay these NABs. However, according to the peer-reviewed medical literature, the clinical utility of these assays has not been established.

**CODES:**

**Important note:**

*CODES: Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.*

CPT Not Covered:	83520 Immunoassay, analyte quantitative; not otherwise specified [if reported for neutralizing antibodies against interferon beta] 87253 - Virus isolation; tissue culture, additional studies or definitive identification (eg, hemabsorption, neutralization, immunofluorescence stain), each isolate 86382 - Neutralization test, viral
ICD-10 Codes	B35 – Multiple Sclerosis



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**CMS:** No NCD or LCD

### POLICY HISTORY:

Status	Date	Action
New	12/28/2010	New policy
Reviewed	12/6/2011	Reviewed
Reviewed	11/15/2012	Reviewed
Reviewed	10/24/2013	No changes
Reviewed	08/21/2014	No changes
Reviewed	08/11/2015	No changes
Reviewed	09/08/2016	Minor updates
Reviewed	08/22/2017	No changes
Reviewed	06/19/2018	No changes
Reviewed	09/26/2019	No changes

### REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. SWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available and they are not included in the list, please forward the reference(s) to SWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Sorensen PS, Ross C, Clemmesen KM et al. Clinical importance of neutralising antibodies against interferon beta in patients with relapsing-remitting multiple sclerosis. *Lancet*. 2003; 362(9391):1184-91.
2. Sorensen PS, Koch-Henriksen N, Ross C et al. Appearance and disappearance of neutralizing antibodies during interferon-beta therapy. *Neurology*. 2005;65(1):33-9.
3. Gneiss C, Reindl M, Lutterotti A et al. Interferon-beta: the neutralizing antibody (NAb) titre predicts reversion to NAb negativity. *Mult Scler*. 2004;10(5):507-10.
4. Giovannoni G, Goodman, A. Neutralizing anti-IFN-beta antibodies: how much more evidence do we need to use them in practice? *Neurology*. 2005;65(1):6-8.
5. Hemmer B, Stuve O, Kieseier B et al. Immune response to immunotherapy: the role of Neutralising antibodies to interferon beta in the treatment of multiple sclerosis. *Lance Neurol*. 2005;4(7):403-12.
6. Petkau AJ, White RA, Ebers GC et al. Longitudinal analyses of the effects of neutralizing antibodies on interferon beta-1b in relapsing-remitting multiple sclerosis. *Mult Scler*. 2004;10(2):126-38.
7. Vartanian T, Solberg Sorensen P, Rice G. Impact of neutralizing antibodies on the clinical efficacy of interferon beta in multiple sclerosis. *J Neurol*. 2004;251 Suppl 2:1125-30.
8. Panitch H, Miller a, Paty D et al. Interferon beta-1b in secondary progressive MS: results from a 3-year controlled study. *Neurology*. 2004;63(10):1788-95.
9. Sorenson PS, Deisenhammer F, Duda P et al. Guidelines on the use of anti-IFN-β antibody measurements in multiple sclerosis: report of an EFNS Task Force on INF-β antibodies in multiple sclerosis. *European Journal of Neurology* 2005;12:817-827.
10. Goodin DS, Frohman EM, Hurwitz B et al. Neutralizing antibodies to interferon beta: Assessment of their clinical and radiographic impact: An evidence report. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2007;68:977-984.
11. Hurwitz BJ Important sources of variability in clinical studies of neutralizing antibodies against interferon beta. *J Neurol Sci*. 2008 Sep 15;272(1-2):8-19. Epub 2008 Jul 11.
12. Wingerchuk DM. Current evidence and therapeutic strategies for multiple sclerosis. *Semin Neurol*. 2008 Feb;28(1):56-58.



Scott & White  
**HEALTH PLAN**  
PART OF BAYLOR SCOTT & WHITE HEALTH

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13. Creeke PI, Farrell RA. Clinical testing for neutralizing antibodies to interferon-B in Multiple Sclerosis. Ther Adv Neurol Disord. 2013 Jan 6(1): 3-17.