Natalizumab for Multiple Sclerosis

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INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage Policy

Note: Natalizumab (Tysabri®) is also indicated for Crohn’s disease. Use for this indication is addressed in a separate coverage policy (Natalizumab for Crohn’s Disease). Please refer to the related coverage policy link above.

Natalizumab (Tysabri®) is considered medically necessary when ALL of the following criteria are met:

- Individual is 18 years of age or older
- Monotherapy treatment of ONE of the following:
  - Active Secondary Progressive Multiple Sclerosis (SPMS) (for example, SPMS with a documented relapse)
  - Clinically Isolated Syndrome
  - Relapsing-Remitting Multiple Sclerosis
- ONE of the following:
  - Documented failure/inadequate response, contraindication per FDA label, intolerance, or not a candidate (for example, stabilized condition where therapeutic interchange is inappropriate) for ONE disease modifying therapy
  - Treatment of highly-active or aggressive multiple sclerosis documented by one of the following:
    - Demonstration of rapidly-advancing deterioration(s) in physical functioning (for example, loss of mobility/or lower levels of ambulation, severe changes in strength or coordination)
    - Documentation of disabling relapse(s) with suboptimal response to systemic corticosteroids
- Magnetic resonance imaging (MRI) findings suggest highly-active or aggressive multiple sclerosis (for example, new, enlarging, or a high burden of T2 lesions or gadolinium-enhancing lesions)
- Documentation of cognitive impairment related to multiple sclerosis (for example, deficits in short-term or long-term memory, visual spatial ability deficits)

- Prescribed by, or in consultation with, a neurologist

Natalizumab (Tysabri) is considered experimental, investigational or unproven for ANY other use including the following:
- Non-Relapsing Forms of Multiple Sclerosis (for example, primary progressive multiple sclerosis)

Initial authorization is up to 12 months.

Reauthorization is up to 12 months when the initial authorization criteria are met.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

**FDA Approved Indications**

**FDA Approved Indication**

**Multiple Sclerosis (MS)**
Tysabri is indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Tysabri increases the risk of PML [see Warnings and Precautions (5.1)]. When initiating and continuing treatment with Tysabri, physicians should consider whether the expected benefit of Tysabri is sufficient to offset this risk.

**Crohn’s Disease (CD)**
Tysabri is indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn’s disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-α. Tysabri should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α [see Warnings and Precautions (5.1)].

**Recommended Dosing**

**FDA Recommended Dosing**
Only prescribers registered in the MS TOUCH® Prescribing Program may prescribe Tysabri for multiple sclerosis. The recommended dose of Tysabri for multiple sclerosis is 300 mg intravenous infusion over one hour every four weeks.

**General Background**

**Disease Overview**
Multiple Sclerosis (MS) is a chronic, inflammatory, demyelinating, autoimmune disease of the central nervous system (CNS) that impacts almost 1,000,000 people in the US. The condition is marked by inflammation and demyelination, as well as degenerative alterations. Patients usually experience relapses and remissions in their neurological symptoms. For most patients, the onset of MS symptoms occurs when patients are 20 to 40 years of age; however, children can get MS and new onset disease can occur in older adults. The MS disease course is heterogeneous but has some patterns. Approximately 85% to 90% of patients have a relapsing pattern at onset. However, this transitions over time in patients who are untreated to a worsening with very few or no relapses or magnetic resonance imaging (MRI) activity (secondary progressive MS). Around 10% to 15% of
patients have a steady progression of symptoms over time (primary progressive MS), marked by some clinical manifestations or by MRI activity. Primary progressive MS is generally diagnosed in patients on the upper level of the typical age range (e.g., almost 40 years of age) and the distribution is equivalent among the two genders. (MS Coalition, 2019)

Advances in the understanding of the MS disease process, as well as in MRI technology, spurred updated disease course descriptions in 2013, as well as in 2017. The revised disease courses are clinically isolated syndrome, relapsing remitting MS, primary progressive MS, and secondary progressive MS. Clinically isolated syndrome is now more recognized among the course descriptions of MS. It is the first clinical presentation of MS that displays characteristics of inflammatory demyelination that may possibly be MS but has yet to fulfill diagnostic criteria. It is notable that the other MS designations can be further characterized considering whether patients have active disease (or not active), as well as if disease is worsening or stable. Disability in MS is commonly graded on the deterioration of mobility per the Expanded Disability Status Scale (EDSS) an ordinal scale that ranges from 0 to 10, with higher scores indicating greater disability. (Lubin, 2013; MS Coalition, 2019; Thompson, 2017)

**Professional Societies/Organizations**

**American Academy of Neurology (AAN)**

The AAN practice guideline recommendations regarding disease-modifying therapies for adults with Multiple Sclerosis (MS) makes distinct recommendations of situations in which preferences may be considered, some of which are medication-related. Evidence supports higher efficacy of Lemtrada, Tysabri, Gilenya, and Ocrevus compared with previously self-injectable disease-modifying MS therapies. Subgroup analyses from Phase III pivotal trials with Lemtrada, Gilenya, and Tysabri demonstrate a reduction in MS relapses and MRI measures in patients with MS who have highly-active disease. Compared with beta interferon therapy, treatment with these agents led to more favorable outcomes in the cohort of patients with MS who have highly active disease. For patients with highly-active MS, use of Lemtrada, Gilenya, or Tysabri should be considered (Level B). With Aubagio, there may be a risk of teratogenicity from male sperm, which may last for 2 years following treatment cessation if the patient does not receive chelation therapy. Men with MS should be counseled regarding their reproductive plans before initiating Aubagio therapy (Level B). Tysabri has been associated with progressive multifocal leukoencephalopathy (PML). Regarding oral products, there are rare reports of PML with both Gilenya and Tecfidera. Patients who are considering therapy with Tysabri, Gilenya, Ocrevus, and Tecfidera should be informed about the risks of PML. (Rae-Grant, 2018a)

The American Board of Internal Medicine’s (ABIM) Foundation Choosing Wisely® Initiative

No recommendations are available for Multiple Sclerosis.

**Centers for Medicare & Medicaid Services - National Coverage Determinations (NCDs)**

There are no CMS National Coverage Determinations for Tysabri.

**Other Covered Uses**

AHFS Drug Information 2020 Edition does not support any off-label uses of Tysabri.

**Experimental, Investigational, Unproven Uses**

**Non-Relapsing Forms of Multiple Sclerosis.** Note: An example of a non-relapsing form of MS is primary progressive MS. The efficacy of Tysabri has not been established in patients with MS with non-relapsing forms of the disease. (Biogen, 2019)

**Coding/Billing Information**

**Note:**

1) This list of codes may not be all-inclusive.

2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

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<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J2323</td>
<td>Injection, natalizumab, 1 mg</td>
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References