

Drug Therapy Guidelines

Tysabri® (natalizumab)

*Applicable**

Medical Benefit	x	Effective: 11/1/18
Pharmacy- Formulary 1		Next Review: 9/19
Pharmacy- Formulary 2		Date of Origin: 1/20/04
Pharmacy- Formulary 3/Exclusive		Review Dates: 1/20/04, 1/18/05, 8/16/05, 10/15/06, 11/28/06,
Pharmacy- Formulary 4/AON		11/5/07, 12/15/08, 12/09, 12/10, 12/11, 12/12, 12/13, 12/14, 9/15, 9/16, 9/17, 9/18

I. Medication Description

Tysabri (natalizumab) is a monoclonal antibody drug designed to block the movement of specific inflammatory cells (leukocytes, except neutrophils) from blood vessels towards areas of inflammation. Tysabri® is an integrin receptor antagonist and classified as a selective adhesion molecule inhibitor which blocks movement of immune cells by attaching to $\alpha 4\beta 1$ -integrins, proteins found on the surface of immune T cells that enable the cells to cross the blood brain barrier. This action interrupts the inflammatory process which may slow disease progression.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage for Tysabri is provided when the following criteria are met:

- For Multiple Sclerosis
 - Prescribing physician must be a neurologist **AND**
 - Member is 18 years of age or older **AND**
 - Member has an active, relapsing form of multiple sclerosis **AND**
 - Member has had an inadequate response to (either by clinical exacerbation or evidence of worsening), or is unable to tolerate alternate disease-modifying multiple sclerosis therapies **AND**
 - Treatment is used as monotherapy (not in combination with any disease-modifying therapy) **AND**
 - Documentation of an MRI scan must be obtained for each member with MS to help differentiate potential, future MS symptoms from PML
- For Crohn's Disease
 - Prescribing physician must be a gastroenterologist **AND**
 - Member is 18 years of age or older **AND**
 - Has moderately to severely active Crohn's disease with evidence of inflammation **AND**
 - Has had an inadequate response to, or is unable to tolerate, conventional Crohn's Disease therapies (corticosteroids, aminosaliclates, methotrexate, azathioprine, 6-mercaptopurine, and/or antibiotics) and at least two inhibitors of TNF- α (Humira, Remicade) **AND**

- Member does not have significantly compromised immune system function either by disease or immunosuppressive therapy **AND**
- Treatment is not in combination with immunosuppressants (6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or TNF-alpha inhibitors. Aminosalicylates may be continued during treatment with Tysabri.

IV. Quantity Limitations

- 300 mg (1 vial, 15 mL) every 4 weeks

V. Coverage Duration

Coverage is provided for 6 months and may be renewed.

VI. Coverage Renewal Criteria

Coverage can be renewed based upon the following criteria:

- For Multiple Sclerosis
 - Member displays a reduction in the accumulation of physical disability and frequency of clinical exacerbations **AND**
 - Absence of unacceptable toxicity from the drug
- For Crohn's Disease
 - Clinical response and remission of disease is maintained with continued use **AND**
 - Member experienced therapeutic benefit by 12 weeks of induction therapy **AND**
 - Member discontinued chronic concomitant steroids within six months of starting therapy **AND**
 - Absence of unacceptable toxicity from the drug

Safety and efficacy for Tysabri has not been established for use longer than four years in patients with MS. The risk of developing progressive multifocal leukoencephalopathy (PML) with natalizumab (Tysabri) use increases with the number of infusions received. Approvals for more than 48 doses will be approved on a case-by-case basis.

VII. Billing/Coding Information

- J2323: 1 billable unit = 1mg
- Available as 300 mg in 15 mL (20 mg/mL) sterile, single-use vial
- Pertinent diagnoses:
 - Multiple Sclerosis: G35
 - Crohn's Disease: K50.00, K50.10, K50.80, K50.90

VIII. Summary of Policy Changes

- 3/1/11: Addition of warnings/precautions section, change in coverage duration from 6 months to 12 months

- 6/15/12: No changes
- 3/15/13:
 - Removal of criteria regarding MS Touch and CD Touch enrollment
 - Change in approval duration for Crohn's Disease to 6 months from 12 months
 - Reduction in warning section to only include Black Box Warnings
- 3/15/14: no policy changes
- 3/15/15: Change in approval duration for all diagnoses to 6 months to correspond with the TOUCH distribution program.
- 7/1/15: formulary distinctions made
- 12/15/15: no policy changes
- 9/15/16: no policy changes
- 10/16/17: no policy changes
- 11/1/18: no policy changes

IX. References

1. Up-to-date Online, retrieved 6/2018.
2. Clinical Pharmacology Online. natalizumab. Elsevier/Gold Standard. Accessed 6/2018.
3. Facts and Comparisons Online, retrieved 8/2017.
4. Tysabri® package insert, Biogen Idec, Inc. Cambridge, MA. Revised 4/2018.
5. Goodin DS, Cohen BA, O'Connor P, Kappos L, Stevens JC. Assessment: the use of natalizumab (Tysabri) for the treatment of multiple sclerosis (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2008 Sep 2;71(10):766-73.
6. Centers for Medicare and Medicaid Services. Medicare Benefit Policy Manual: Chapter 15. (CMS Publication No. 100-02). Retrieved from <http://www.cms.hhs.gov>.

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.

**These guidelines are not applicable to benefits covered under Medicare Advantage. Medicare Advantage benefit coverage requests are reviewed in accordance with the guidance set forth in Chapter 15 Section 50 of the Centers for Medicare & Medicaid Services Medicare Benefit Policy Manual.*