



PHARMACY POLICY STATEMENT

HAP CareSource™ Marketplace

DRUG NAME	Tysabri (natalizumab)
BENEFIT TYPE	Medical
STATUS	Prior Authorization Required

Tysabri, approved by the FDA in 2004, is an integrin receptor antagonist indicated for multiple sclerosis (MS) and Crohn's disease (CD). For the treatment of MS, it is used 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 progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. When initiating and continuing treatment, physicians should consider whether the expected benefit of is sufficient to offset this risk. Tysabri has a black box warning for PML and is only available through a REMS program.

For the treatment of CD, Tysabri is used to induce and maintain 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 . It should not be used in combination with immunosuppressants or inhibitors of TNF- α , and treatment should be discontinued if therapeutic benefit has not been experienced by 12 weeks.

Tysabri (natalizumab) will be considered for coverage when the following criteria are met:

Multiple Sclerosis (MS)

For **initial** authorization:

1. Member must be at least 18 years of age; AND
2. Medication must be prescribed by, or in consultation with, a neurologist; AND
3. Member has a diagnosis of clinically isolated syndrome, relapsing-remitting disease, or active secondary progressive disease; AND
4. Member has documentation of at least one of the following:
 - a) Inadequate response to two or more drugs indicated for the treatment of MS
 - b) Highly active disease (aggressive or rapidly evolving) in the expert opinion of the prescriber.
5. **Dosage allowed/Quantity limit:** 300 mg intravenous infusion every 4 weeks. (1 vial per 28 days).

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:

1. Chart notes must document positive clinical response such as improved disability, slowed progression of disability, or decreased frequency of relapses compared to baseline.

If all the above requirements are met, the medication will be approved for an additional 12 months.



Crohn's Disease (CD)

For **initial** authorization:

1. Member must be at least 18 years of age; AND
2. Medication must be prescribed by or in consultation with a gastroenterologist; AND
3. Member has a documented diagnosis of moderately to severely active CD; AND
4. Member has had a documented trial and inadequate response, or intolerance to at least one of the following conventional therapies: a 4-week trial of a corticosteroid OR a 12-week trial of 6-mercaptopurine, azathioprine, or methotrexate. Note: Trial is not required if member is switching from another biologic agent; AND
5. Member has tried and failed an anti-TNF drug (e.g., Cimzia, Humira, Remicade) unless not tolerated or contraindicated. Note: trial is not required if member has multiple sclerosis and CD; AND
6. Medication is not being used in combination with immunosuppressants or TNF-alpha inhibitors.
7. **Dosage allowed/Quantity limit:** 300 mg intravenous infusion every 4 weeks. (1 vial per 28 days).

If all the above requirements are met, the medication will be approved for 3 months.

For **reauthorization**:

1. Chart notes have been provided showing improvement in signs and symptoms of CD (defined as mucosal healing, fewer flare-ups of symptoms, ability to taper off corticosteroid, etc.).

If all the above requirements are met, the medication will be approved for an additional 12 months.

HAP CareSource considers Tysabri (natalizumab) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
05/10/2017	New policy for Tysabri created. Policy SRx-0041 archived. For diagnosis of CD: trial of Humira required. For RRMS and SPMS diagnoses trial of two formulary agents required. List of diagnoses considered not medically necessary was added.
12/06/2017	Age coverage expanded.
02/26/2019	Humira trial removed from criteria for CD.
11/23/2020	For CD: Changed the trial to only ask for 1 conventional therapy rather than 2. Also added a trial of an anti-TNF in accordance with package insert and guidelines. Changed initial auth to 3 months to observe benefit (must discontinue if no benefit after 3 months).
07/15/2022	Transferred to new template. MS: Updated and added references. Specified types of MS indicated. Added highly active disease option as alternative to trying 2 other drugs first. Specified that the JCV test should be negative. Added clinical criteria for renewal. CD: Added ability to taper off steroids as option to meet renewal criteria.
11/16/2023	Removed JCV antibody test requirement.



References:

1. Tysabri [package insert]. Cambridge, MA; Biogen, Inc.; 2023.
2. Sulz MC, Burri E, Michetti P, et al. Treatment Algorithms for Crohn's Disease. *Digestion*. 2020;101 Suppl 1:43-57.
3. Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2018;113(4):481-517.
4. Torres J, Bonovas S, Doherty G, et al. ECCO Guidelines on Therapeutics in Crohn's Disease: Medical Treatment. *J Crohns Colitis*. 2020;14(1):4-22.
5. Pimentel AM, Rocha R, Santana GO. Crohn's disease of esophagus, stomach and duodenum. *World J Gastrointest Pharmacol Ther*. 2019;10(2):35-49.
6. Terdiman JP, Gruss CB, Heidelbaugh JJ, Sultan S, Falck-Ytter YT; AGA Institute Clinical Practice and Quality Management Committee. American Gastroenterological Association Institute guideline on the use of thiopurines, methotrexate, and anti-TNF- α biologic drugs for the induction and maintenance of remission in inflammatory Crohn's disease. *Gastroenterology*. 2013;145(6):1459-1463.
7. Regueiro M, Velayos F, Greer JB, et al. American Gastroenterological Association Institute Technical Review on the Management of Crohn's Disease After Surgical Resection. *Gastroenterology*. 2017;152(1):277-295.e3.
8. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology [published correction appears in *Neurology*. 2019 Jan 8;92(2):112]. *Neurology*. 2018;90(17):777-788
9. National Multiple Sclerosis Society. The Use of Disease-Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence. A Consensus Paper by the Multiple Sclerosis Coalition; 2019. Available from: https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/DMT_Consensus_MS_Coalition.pdf. Accessed August 18, 2021.
10. Hauser SL, Cree BAC. Treatment of Multiple Sclerosis: A Review. *Am J Med*. 2020;133(12):1380-1390.e2. doi:10.1016/j.amjmed.2020.05.049
11. McGinley MP, Goldschmidt CH, Rae-Grant AD. Diagnosis and Treatment of Multiple Sclerosis: A Review [published correction appears in *JAMA*. 2021 Jun 1;325(21):2211]. *JAMA*. 2021;325(8):765-779. doi:10.1001/jama.2020.26858
12. Polman CH, O'Connor PW, Havrdova E, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. *N Engl J Med*. 2006;354(9):899-910. doi:10.1056/NEJMoa044397
13. Butzkueven H, Kappos L, Wiendl H, et al. Long-term safety and effectiveness of natalizumab treatment in clinical practice: 10 years of real-world data from the Tysabri Observational Program (TOP). *J Neurol Neurosurg Psychiatry*. 2020;91(6):660-668. doi:10.1136/jnnp-2019-322326

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