MAGELLAN PHARMACY SOLUTIONS | icore HEALTHCARE				**Tysabri (natalizumab) (Intravenous)**
Last Review Date: 03/25/2014 **Effective Date of Guideline:** 11/28/2011				**Dates Reviewed:** 12/13/2011, 08/22/2012, 02/07/2013, 06/06/2013, 06/25/2013, 09/05/2013, 12/05/2013, 03/25/2014
Prior Auth Available:	√	**Post-service edit:**	√	**Medical Necessity Criteria Number**: IC-0133

These medical necessity criteria were developed by ICORE Healthcare for the purpose of making clinical review determinations for requests for medications commonly used in various diseases. The developers of the criteria sets included representatives from the disciplines of oncology, hematology, rheumatology, neurology, internal medicine, nursing, and pharmacy were consulted as part of the criteria development. The development followed an extensive literature search pertaining to established clinical guidelines and accepted prescribing patterns for each individual drug. The indications for the medications are generally consistent with the National Comprehensive Cancer Network (NCCN) guidelines, FDA labeling, CMS coverage guidelines, or other published peer reviewed research literature.

I. Medication Description:

Natalizumab is a recombinant humanized immunoglobulin G4-kappa monoclonal antibody produced in murine myeloma cells. Natalizumab binds to the alpha-4 subunit of alpha-4 beta-1 and alpha-4 beta-7 integrins expressed on the surface of all leukocytes except neutrophils and inhibits the alpha-4–mediated adhesion of leukocytes to their counter-receptor(s). The receptors for the alpha-4 family of integrins include vascular cell adhesion molecule 1 (VCAM-1), which is expressed on activated vascular endothelium, and mucosal addressin cell adhesion molecule 1 (MAdCAM-1) present on vascular endothelial cells of the GI tract. Disruption of these molecular interactions prevents transmigration of leukocytes across the endothelium into inflamed parenchymal tissue. In vitro, anti–alpha-4 integrin antibodies also block alpha-4–mediated cell binding to ligands, such as osteopontin and an alternatively spliced domain of fibronectin, connecting segment 1. In vivo, natalizumab may further act to inhibit the interaction of alpha-4–expressing leukocytes with their ligand(s) in the extracellular matrix and on parenchymal cells, thereby inhibiting further recruitment and inflammatory activity of activated immune cells.

II. Length of Authorization:

Crohn's Disease: Initial Treatment is 12 weeks and is eligible for renewal; Renewals will be for 6 months
Multiple Sclerosis: Coverage will be for 6 months and is eligible for renewal.

III. Review Criteria:

- Patient is at least 18 years or older; **AND**

Multiple Sclerosis

- Patient has diagnosis of relapsing-remitting MS(RRMS), secondary progressive MS (SPMS) with relapses or progressive relapsing MS (PRMS); **AND**
- Confirmed diagnosis of MS as documented by laboratory report (i.e. MRI); **AND**
- Documented negative JCV antibody ELISA testiwithin the past 6 months; **AND**
- Prescriber and patient must be enrolled in and meet the conditions of the MS TOUCH program; **AND**
- Documented failure, contraindicated, or ineffective response to a minimum (3) month trial on previous therapy with an interferon beta product (i.e. Avonex, Rebif, Betaseron, Extavia) AND Copaxone; **AND**
- Must beused as single agent therapy

Crohn's Disease Diagnosis

- Patient has moderate to severe active disease; **AND**
- Documented trial and failure on ONE oral immunosuppressive therapy for at least 3 months, unless use is contraindicated, such as corticosteroids, methotrexate, azathioprine, and/or 6-mercaptopurine; **AND**
- Documented trial and failure on ONE TNF-Inhibitor therapy for at least 3 months, unless contraindicated, such as Remicade® (infliximab), Cimzia® (certolizumab, or Humira® (adalimumab); **AND**
- Prescriber and patient must be enrolled in and meet the conditions of the CD TOUCH program; **AND**
- Used as single agent therapy (Not used concurrently with another TNF inhibitor, 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate)

IV. Renewal Criteria:

Authorizations can be renewed based on the following criteria:

- Patient continues to meet criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: hypersensitivity reactions; hepatoxicity; signs or symptoms of progressive multifocal leukoencephalopathy (PML); development of severe infections (including pneumonias, pneumocystis carinii pneumonia, pulmonary mycobacterium avium intracellulare, bronchopulmonary aspergillosis, herpes, urinary tract, gastroenteritis, vaginal, tonsillitis); **AND**

MS Diagnosis

- Adequate documentation of disease stability and/or improvement (i.e., EDSS scores, no relapse, and/or chart notes)

Crohn's Disease Diagnosis

- Clinical response and remission of disease is seen by 12 weeks; **AND**
- Patient has been tapered off of oral corticosteroids within six months of starting Tysabri; **AND**
- Patient does not require additional steroid use that exceeds three months in a calendar year to control their Crohn's disease

V. Dosage/Administration:

Indication	Dose
All Indications	300 mg intravenous infusion over one hour every four weeks

VI. Billing/Code Information:

JCode:

J2323 – Tysabri (Biogen Idec Inc) 300mg injection: 1 billable unit = 1mg

NDC

Tysabri 300 mg/ 15ml - 64406-0008-xx (Biogen Idec Inc)

Max Units (per dose and overtime):

Male: 300 billable units every 28 days (4 weeks)

Female: 300 billable units every 28 days (4 weeks)

Quantity Limitations:

Tysabri 300 mg: 1 injection every 28 days

Covered Diagnosis:

ICD-9 Codes	Diagnosis
340	Multiple sclerosis
555.0	Regional enteritis of small intestine
555.1	Regional enteritis of large intestine
555.2	Regional enteritis of small intestine with large intestine
555.9	Regional enteritis of unspecified site

VII. Centers for Medicare and Medicaid Services (CMS):

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

Jurisdiction(s): 5, 8	**NCD/LCD Document (s):** L32013
ICD-9 Codes	**Diagnosis**
340	Multiple sclerosis
555.0	Regional enteritis of small intestine
555.1	Regional enteritis of large intestine
555.2	Regional enteritis of small intestine with large intestine
555.9	Regional enteritis of unspecified site

VIII. Policy Exclusions:

- Treatment for diagnoses not FDA approved
- All indications not described in Section III Review criteria are not covered and may be considered experimental or investigational.

IX. Black Box Warnings/Contraindications:

Black Box Warnings

- Tysabri increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability.
- Monitor patients, and withold Tysabri immediately at the first sign or symptom suggestive of PML.

- Tysabri is available only through a special restricted distribution program called the TOUCH® Prescribing Program and must be administered only to patients enrolled in this program.

Contraindications:

- Patients who have or have had PML
- Patients who have had a hypersensitivity reaction to Tysabri

X. References:

1. Tysabri [package Insert]. Cambridge, MA; Biogen Idec, Inc.; December 2013. Accessed March 2014.
2. Goodin DS, Cohen BA, O'Connor P, et al. 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; 71:766.
3. Gawronski KM, Rainka MM, Patel MJ, Gengo FM. Treatment Options for Multiple Sclerosis: Current and Emerging Therapies. Pharmacotherapy. 2010;30(9):916-927.
4. Goodin DS, Frohman EM, Garmany GP Jr, et al. Disease modifying therapies in multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology. 2002 Jan 22;58(2):169-78.
5. Lichtenstein GR, Hanauer SB, Sandborn WJ, Practice Parameters Committee of American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol. 2009;104(2):465.
6. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Drugs and Biologics (Non-chemotherapy) (L32013). Centers for Medicare & Medicaid Services, Inc. Updated on 10/22/2013 with effective date 11/15/2013. Accessed March 2014.

XI. Appendix:

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E	CA,HI, NV, AS, GU, CNMI	Noridian Administrative Services (NAS)
F	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Administrative Services (NAS)
5	KS, NE, IA, MO	Wisconsin Physicians Service (WPS)
6	MN, WI, IL	National Government Services (NGS)
H	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions
8	MI, IN	Wisconsin Physicians Service (WPS)
9 (N)	FL, PR, VI	First Coast Service Options
10 (J)	TN, GA, AL	Cahaba Government Benefit Administrators
11 (M)	NC, SC, VA, WV	Palmetto GBA
12 (L)	DE, MD, PA, NJ, DC	Novitas Solutions
K	NY, CT, MA, RI, VT, ME, NH	National Government Services (NGS)
15	KY, OH	CGS Administrators, LLC