Tysabri® (natalizumab)
(Intravenous)

Document Number: IC-0133

Last Review Date: 10/02/2018
Date of Origin: 11/28/2011
Dates Reviewed: 12/2011, 08/2012, 02/2013, 06/2013, 06/2013, 09/2013, 12/2013, 03/2014, 06/2014, 09/2014, 01/2015, 02/2015, 06/2015, 09/2015, 12/2015, 03/2016, 06/2016, 09/2016, 12/2016, 03/2017, 06/2017, 09/2017, 12/2017, 03/2018, 06/2018, 10/2018

I. Length of Authorization

Crohn's Disease:

- Coverage is eligible for renewal
  - Initial coverage will be provided for 12 weeks
  - Renewal coverage will be provided for 6 months

Multiple Sclerosis:

- Coverage will be provided for 6 months and is eligible for renewal.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

– Tysabri 300 mg/15 mL vial for injection: 1 vial per 28 days

B. Max Units (per dose and over time) [Medical Benefit]:

- 300 billable units every 28 days

III. Initial Approval Criteria

- Patient is at least 18 years old; **AND**
- Prescriber and patient must be enrolled in and meet the conditions of the TOUCH program; **AND**
- Documented negative JCV antibody ELISA test within the past 6 months§; **AND**
- Not used in combination with antineoplastic, immunosuppressant, or immunomodulating agents; **AND**

Multiple Sclerosis †

- Patient has been diagnosed* with a relapsing form of multiple sclerosis [i.e. relapsing-remitting disease (RRMS) or secondary progressive disease (SPMS) with relapses]; **AND**
- Confirmed diagnosis* of MS as documented by laboratory report (i.e. MRI); **AND**
- Must be used as single agent therapy

Crohn's Disease †

- Patient has moderate to severe active disease; **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool; **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 infliximab, certolizumab, or adalimumab; **AND**
- Used as single agent therapy [Not used concurrently with another biologic drug or immunosuppressant (e.g., 6-mercaptopurine, azathioprine, cyclosporine, methotrexate, etc.) used for Crohn's Disease]

† FDA Approved Indication(s)

***Definitive diagnosis of MS with a relapsing-remitting course is based upon BOTH dissemination in time and space. Unless contraindicated, MRI should be obtained (even if criteria are met).**

Dissemination in time *(Development/appearance of new CNS lesions over time)*	**Dissemination in space** *(Development of lesions in distinct anatomical locations within the CNS; multifocal)*

• ≥ 2 clinical attacks; **OR**
• 1 clinical attack AND one of the following:
  ○ MRI indicating simultaneous presence of gadolinium-enhancing and non-enhancing lesions at any time or by a new T2-hyperintense or gadolinium-enhancing lesion on follow-up MRI compared to baseline scan
  ○ CSF-specific oligoclonal bands
	• ≥ 2 lesions; **OR**
	• 1 lesion AND one of the following:
	  ○ Clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location
	  ○ MRI indicating ≥ 1 T2-hyperintense lesions characteristic of MS in ≥ 2 of 4 areas of the CNS (periventricular, cortical or juxtacortical, infratentorial, or spinal cord)

§ Risk factors for the development of Progressive Multifocal Leukoencephalopathy (PML) [13,14]

- Presence of anti-JCV antibodies
- Prior treatment with an immunosuppressant
- Natalizumab treatment, especially beyond 2 years
- Elevated levels of anti-JCV antibody response index (i.e., index > 0.9)*

** In those using natalizumab for 25–36 months with no prior use of immunosuppressants, the PML risk is 0.2 per 1,000 in those with an index of 0.9 or less, 0.3 per 1,000 in those with an index of 0.9–1.5, and 3 per 1,000 in those with an index greater than 1.5.*

IV. Renewal Criteria

Authorizations can be renewed based on the following criteria:

- Patient continues to meet the criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: hypersensitivity reactions, hepatotoxicity, 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 infections, gastroenteritis, vaginitis, tonsillitis, meningitis), etc.; **AND**
- Documented negative JCV antibody ELISA test within the past 6 months; **AND**

Multiple Sclerosis

- Continuous monitoring of response to therapy [manifestations of MS disease activity include, but are not limited to, an increase in annualized relapse rate (ARR), development of new/worsening T2 hyperintensities or enhancing lesions on brain/spinal MRI, and progression of sustained impairment as evidenced by expanded disability status scale (EDSS), timed 25-foot walk (T25-FW), 9-hole peg test (9-HPT)]
  - Inadequate response, in those who have been adherent and receiving therapy for sufficient time to realize the full treatment effect, is defined as ≥ 1 relapse, ≥ 2 unequivocally new MRI-detected lesions, or increased disability on examination over a one-year period
  - Infusion reactions or breakthrough disease activity may indicate neutralizing natalizumab antibodies. Therapy should be discontinued in patients who have persistent neutralizing antibodies to natalizumab

Crohn's Disease

- Initial renewal only:
  - Clinical response and remission of disease is seen by 12 weeks
- Second renewal only:
  - Patient has been tapered off of oral corticosteroids within six months of starting Tysabri; **AND**
  - Disease response as indicated by improvement in signs and symptoms compared to baseline such as endoscopic activity, number of liquid stools, presence and severity of abdominal pain, presence of abdominal mass, body weight compared to IBW, hematocrit, presence of extra intestinal complications, tapering or discontinuation of corticosteroid

therapy, use of anti-diarrheal drugs, and/or an improvement on a disease activity scoring tool [e.g. an improvement on the Crohn's Disease Activity Index (CDAI) score or the Harvey-Bradshaw Index score.]

- All subsequent renewals:
  - Patient does not require additional steroid use that exceeds three months in a calendar year to control their Crohn's disease; **AND**
  - Disease response as indicated by improvement in signs and symptoms compared to baseline such as endoscopic activity, number of liquid stools, presence and severity of abdominal pain, presence of abdominal mass, body weight compared to IBW, hematocrit, presence of extra intestinal complications, tapering or discontinuation of corticosteroid therapy, use of anti-diarrheal drugs, and/or an improvement on a disease activity scoring tool [e.g. an improvement on the Crohn's Disease Activity Index (CDAI) score or the Harvey-Bradshaw Index score.]

V. Dosage/Administration

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

VI. Billing Code/Availability Information

JCode:

- J2323 – Injection, natalizumab, 1 mg; 1 billable unit = 1mg

NDC:

- Tysabri 300 mg/15 mL single-use vial: 64406-0008-xx

VII. References

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G35	Multiple Sclerosis
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction

ICD-10	ICD-10 Description
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications

Appendix 2 – 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):** L34741
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L34741&bc=gAAAAAAAAAAAAA==	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC