CLINICAL MEDICATION POLICY	
Policy Name:	Tysabri® (natalizumab)
Policy Number:	MP-008-MC-ALL
Responsible Departments:	Medical Management, Medical Policy, Clinical Pharmacy
Provider Notice Date:	04/1/2017
Original Effective Date:	05/01/2017
Annual Approval Date:	03/15/2018
Revision Date:	N/A
Products:	Ohio Medicare Assured
Application:	All participating and nonparticipating hospitals and providers
Page Number(s):	1 of 7

Disclaimer

Gateway Health℠ (Gateway) clinical medication policy is intended to serve only as a general reference resource regarding payment and coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Gateway Health℠ may provide coverage under the medical or pharmacy benefits of the Company's Medicare products for medically necessary Tysabri (natalizumab) intravenous administration.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

DEFINITIONS

Progressive multifocal leukoencephalopathy (PML) – An opportunistic viral infection of the brain that usually leads to death or severe disability.

Relapsing-remitting multiple sclerosis (RRMS) – Primary form of multiple sclerosis (MS) that occurs in approximately 85% of patients, characterized by acute attacks followed by periods of remission.

Secondary-progressive multiple sclerosis (SPMS) – An initial period of RRMS, followed by a steadily progressive course, with or without acute relapses; 75-85% of patients diagnosed with RRMS will transition to SPMS.

Progressive-relapsing multiple sclerosis (PRMS) – Steadily progressive course from onset with acute attacks, with or without recovery; occurs in less than 5% of MS patients.

Crohn's Disease – A chronic inflammatory bowel disease that affects both men and women.

PROCEDURES

1. Tysabri (natalizumab) is considered medically necessary as an intravenous infusion for:

    A. The treatment of relapsing forms of multiple sclerosis (MS) when the patient meets all of the following criteria:
        1) Patient is 18 years of age and older; AND
        2) Documentation of a diagnosis of relapsing-remitting or relapsing secondary progressive MS; AND
        3) The drug is given as monotherapy and not in combination with other therapies approved for the treatment of MS; AND
        4) Must be prescribed by, or in consultation with, a neurologist or a physician that specializes in the treatment of MS; AND
        5) Patients initiating therapy for the first time must have at least one clinical relapse documented (e.g., functional disability, hospitalization, acute steroid therapy, etc.) during the prior year; AND
        6) Therapeutic failure or an inadequate response to two or more medications indicated for the treatment of MS; AND
        7) Chart documentation provided that demonstrates ongoing monitoring and evaluation of transaminase and bilirubin levels; AND
        8) Documentation of a baseline MRI scan provided to evaluate for pre-existing progressive multifocal leukoencephalopathy (PML) and done annually while on treatment; AND
        9) Patient has had anti-JCV antibody testing prior to initiating treatment and annually; AND
        10) Coverage provided for situations in which there is functional status that can be preserved. Patient must still either be able to walk at least a few steps or alternatively must have some functional arm/hand use consistent with performing activities of daily living; AND
        11) Provider, patient, and pharmacy must be enrolled in the MS TOUCH REMS Prescribing Program; AND
        12) Dose must not exceed FDA labeled 300 mg infused IV once monthly; AND
        13) Administration of the medication must be done by a health care provider; AND
        14) Reauthorization requires documentation of the following:

a. Documentation of a clinical response (decrease in CDAI from baseline);
b. No evidence of liver impairment indicated by jaundice or elevated laboratory markers (transaminase, bilirubin);
c. No evidence of PML;
d. If being prescribed for longer than 2 years, documentation the patient has been educated and understands the risk versus benefit of continuing therapy

B. The treatment of moderate to severe Crohn's disease when the patient meets all of the following criteria:
   1) Patient is 18 years of age or older; AND
   2) Must be prescribed by, or in consultation with, a gastroenterologist; AND
   3) The drug is given as monotherapy and NOT being used in combination with immunosuppressants or inhibitors of TNF-α; AND
   4) Patient has had anti-JCV antibody testing prior to initiating treatment and annually thereafter; AND
   5) Prescriber and patient must be enrolled in CD TOUCH REMS Prescribing Program; AND
   6) Documentation of elevated C-reactive protein (evidence of inflammation) and baseline Crohn's Disease Activity Index ≥ 220 (moderate to severe disease); AND
   7) Must have an inadequate response or intolerance/contraindication to at least 1 medication from each of the following classes:
      a. Aminosalicylates (sulfasalazine, mesalamine)
      b. Corticosteroids (budesonide, prednisone)
      c. Immunomodulators (Azathioprine, 6-mercaptopurine, methotrexate)
      d. TNF-α inhibitors (adalimumab, infliximab); AND
   8) Dose must not exceed FDA labeled 300 mg infused IV once monthly; AND
   9) Administration of the medication must be done by a health care provider; AND
   10) Reauthorization requires documentation of the following:
      a. Documentation of a clinical response (decrease in CDAI from baseline);
      b. No evidence of liver impairment indicated by jaundice or elevated laboratory markers (transaminase, bilirubin);
      c. No evidence of PML;
      d. If being prescribed for longer than 2 years, documentation the patient has been educated and understands the risk versus benefit of continuing therapy

2. Contraindications
   Natalizumab is contraindicated in patients who have or have had progressive multifocal leukoencephalopathy (PML) and in patients who have had a hypersensitivity reaction to natalizumab.

3. When Tysabri is not covered
   A. Patients with pre-existing hepatic disease or hepatic impairment defined as ALT or AST at least two times the ULN; OR
   B. Combination use with oral corticosteroids that cannot be tapered off within 6 months of starting Tysabri; OR
   C. In Crohn's disease, Tysabri should not be used in combination with immunosuppressants or inhibitors of TNF-α;
   D. For conditions other than those listed above because the scientific evidence has not been established.

   Coverage may be provided for any non-FDA labeled indication if it is determined that the use is a medically accepted indication supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis(es) for which it is prescribed. These requests will be reviewed on a case-by-case basis to determine medical necessity.

   When criteria are not met, the request will be forwarded to a Medical Director for review. The physician reviewer must override criteria when, in their professional judgment, the requested medication is medically necessary.

4. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Gateway Health℠ at any time pursuant to the terms of your provider agreement.

5. Place of Service
   The place of service for the intravenous administration of Tysabri (natalizumab) is outpatient.

6. Coverage Determination
   Gateway Health℠ follows the coverage determinations made by CMS as outlined in either the national coverage determinations (NCD) or the state-specific local carrier determination (LCD).

   There is no specific NCD for this medication. For Ohio, CGS, the local carrier, does not have a specific LCD for Tysabri. For additional information, please see: http://www.cgsmedicare.com/partb/medicalpolicy/index.html

Governing Bodies Approval
The FDA approved Tysabri on November 23, 2004 as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. Tysabri increases the risk of PML. When initiating and continuing treatment with Tysabri, physicians should consider whether the expected benefit of Tysabri is sufficient to offset this risk.

The FDA approved Tysabri on January 15, 2008 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.

CODING REQUIREMENTS

Procedure Codes

CPT/HCPCS Codes	Description
J2323	Solution for Injection, Natalizumab, 300mg/15mL

Diagnosis Codes

ICD-10 Code	Description
G35.0	Multiple Sclerosis (relapsing-remitting)
K50.00	Crohn's disease of small intestine with complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
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 complications
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.11	Crohn's disease of large intestine with 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 complications
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine with 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 complications
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified
K50.91	Crohn's disease, 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 complications

K50.919	Crohn's disease, unspecified, with unspecified with unspecified complications

REMBURSEMENT

Participating facilities will be reimbursed per their Gateway Health℠ contract.

POLICY SOURCE(S)

Tysabri® (Natalizumab) [package insert]. Cambridge, MA: Biogen; 05/2016. Accessed on December 13, 2016 and available at: https://www.tysabri.com/content/dam/commercial/multiple-sclerosis/tysabri/pat/en_us/pdfs/tysabri_prescribing_information.pdf

Tysabri®. In: Micromedex 2.0 online. Ann Arbor, MI. Truven Health Analytics; 2016. Accessed December 13, 2016.

Disease-modifying treatment of relapsing-remitting multiple sclerosis in adults. Up-to-date, July 2016. Accessed July 11, 2016.

National Multiple Sclerosis Society. Accessed December 14, 2016 and available at: http://www.nationalmssociety.org/index.aspx .

Lichtenstein GA, Hannauer SB, Sandborn WJ, et al. Management of Crohn's Disease in Adults. American College of Gastroenterology Practice Guidelines. Am J Gastroenterol advance online publication, 6 January 2009; doi: 10.1038/ajg.2008.168. Accessed online on December 15, 2016 and available at: http://www.nature.com/ajg/journal/v104/n2/full/ajg2008168a.html

Terdiman J, Gruss C, Heidelbaugh JJ, et al. 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. 20163 Dec; 145(6): 1459-63. Accessed on March 9, 2017 and available at: https://www.guideline.gov/summaries/summary/47784

Policy History:

Date	Activity
N/A	LCD/NCD effective date
03/15/2017	QI/UM Committee approval
05/01/2017	Provider effective date