MEDICAL MUTUAL®

Drug Policy

Policy:	**201305**	**Initial Effective Date: 01/16/2013**
Code(s):	**HCPCS J2323**	**Annual Review Date: 8/16/2018**
SUBJECT:	**Tysabri (natalizumab)**	**Last Revised Date: 8/16/2018**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

OVERVIEW

Natalizumab (Tysabri®, Biogen Idec, Inc., Cambridge, MA), is a recombinant humanized IgG4κ monoclonal antibody produced in murine myeloma cells. The specific mechanism(s) by which natalizumab exerts its effects in multiple sclerosis (MS) and Crohn's disease have not been fully defined. In relapsing forms of multiple sclerosis, the drug has been shown to reduce relapses and the appearance of new brain lesions. Natalizumab is also utilized for treatment of moderately to severely active Crohn's disease.

POLICY STATEMENT

This policy involves the use of Tysabri. Prior authorization is recommended for pharmacy and medical benefit coverage of Tysabri. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Tysabri as well as the monitoring required for AEs and long-term efficacy, initial approval requires Tysabri be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

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RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Tysabri (natalizumab) is recommended in those who meet the following criteria:

1. Relapsing Form of Multiple Sclerosis (MS) in an Adult.

Criteria. *Approve in patients who meet the following criteria (A, B, C, D, and E)*:
A) The patient is ≥ 18 years of age; AND
B) The patient has a relapsing form of MS (relapsing forms of MS are Relapsing-remitting MS, Secondary-progressive MS with relapses, and Progressive-relapsing MS); AND
C) Failure of (trial of ≥1 month per drug), intolerance to or unable to receive (e.g., interferon not recommended in an individual with depression/mood disorder) ***at least one*** therapeutic agent from ***two or more*** of the following drug categories OR have highly active/aggressive MS (highly active/aggressive MS requires documented features such as: frequent and/or severe relapses, incomplete recovery from relapses, early accrual of physical or cognitive impairment, heavy burden of MRI T2 lesions, multiple enhancing lesions at onset, high burden of gadolinium enhancing lesions, or early brain atrophy) :
    1. Interferon beta-1a (e.g., Avonex®, Plegridy®, Rebif®) or interferon beta-1b (e.g., Betaseron®, Extavia®); or
    2. Glatiramer acetate (Copaxone®, Glatopa™); or
    3. Fingolimod (Gilenya®); or
    4. Teriflunomide (Aubagio®); or
    5. Dimethyl fumarate (Tecfidera®); or
    6. Alemtuzumab (Lemtrada®); or
    7. Daclizumab (Zinbryta®);or
    8. Ocrelizumab (Ocrevus).
D) Natalizumab will not be used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, methotrexate) or other disease-modifying agents (e.g., interferon beta-1a, interferon beta-1b, glatiramer acetate); AND
E) Natalizumab is prescribed by, or in consultation with, a physician who specializes in the treatment of multiple sclerosis (MS) and/or a neurologist.

Dosing in Tysabri. *Dosing must meet the following:* 300 mg intravenous infusion every 4 weeks

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months
B) *Extended Approval:* 1 year

Duration of Therapy in Multiple Sclerosis (MS): Indefinite.

It is thought that the incidence of PML increases with increasing duration of therapy and most patients receive Tysabri for 2 to 3 years.

Labs/Diagnostics. None required.

2. Crohn's Disease in an Adult.

Criteria.
For Crohn's Disease- induction of remission of moderate to severe, Approve in patients who meet the following criteria (A, B, C, D, E, F, G, and H).
For Crohn's Disease - maintenance of remission of moderate to severe, Approve in patients who meet the following criteria (A, B, E, F, G, and H).

- **A)** The patient is ≥ 18 years of age; AND
- **B)** Prescriber has assessed baseline disease severity using an objective measure/tool; AND
- **C)** Coverage is provided for patients who have experienced failure of, intolerance to or are unable to receive aminosalicylates (e.g., sulfasalazine, mesalamine, balsalazide); AND
- **D)** Coverage is provided for patients who have experienced failure of, intolerance to or are unable to receive corticosteroids (e.g., prednisone); AND
- **E)** Coverage is provided for patients who have experienced failure of, intolerance to or are unable to receive immunomodulators (e.g., azathioprine, 6-mercaptopurine, methotrexate).; AND
- **F)** Coverage is provided for patients who have experienced failure of a 2 month trial, intolerance to or are unable to receive AT LEAST TWO TNF-α inhibitors (e.g., adalimumab, certolizumab pegol, infliximab); AND
- **G)** Natalizumab will not be used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, methotrexate) or TNF-α inhibitors (e.g., adalimumab [Humira], certolizumab pegol[Cimzia], infliximab[Remicade or Inflectra]); AND
- **H)** Natalizumab is prescribed by or in consultation with a gastroenterologist.

Dosing in Tysabri. *Dosing must meet the following:* 300 mg intravenous infusion every 4 weeks

Initial Approval/ Extended Approval.
A) *Initial Approval:* 3 months
B) *Extended Approval:* 1 year

Duration of Therapy in Crohn's Disease. Indefinite.

Labs/Diagnostics. None required.

3. Patient has been Started on Tysabri.
Criteria.
For Relapsing Form of Multiple Sclerosis (MS) in an Adult- The patient must meet the following criteria (A, B, C, D, E, F,and G):

- **A)** The patient has a history of beneficial response to Natalizumab; AND
- **B)** The patient is ≥ 18 years of age; AND
- **C)** The patient has a relapsing form of MS (relapsing forms of MS are Relapsing-remitting MS, Secondary-progressive MS with relapses, and Progressive-relapsing MS); AND

D) Natalizumab will not be used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, methotrexate) or other disease-modifying agents (e.g., interferon beta-1a, interferon beta-1b, glatiramer acetate); AND
E) Natalizumab is prescribed by, or in consultation with, a physician who specializes in the treatment of multiple sclerosis (MS) and/or a neurologist; AND
F) Dosage and administration are consistent with U.S. Food and Drug Administration approved label (i.e., 300 mg intravenous infusion every four weeks.); AND
G) Provider attests to the absence of toxicity from natalizumab (such as progressive multifocal leukoencephalopathy (PML) severe infections, etc.) as well as monitoring for JCV antibodies.

For Crohn's Disease- The patient must meet the following criteria (A, B, C, D, E, F, and G).

A) The patient has a history of beneficial response to natalizumab (such as an indication 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 ideal body weight (IBW), hematocrit, presence of extra intestinal complications, 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.]; AND
B) The patient is ≥ 18 years of age; AND
C) Natalizumab will not be used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, methotrexate) or TNF-α inhibitors (e.g., adalimumab [Humira], certolizumab pegol[Cimzia], infliximab[Remicade or Inflectra]); AND
D) Natalizumab is prescribed by or in consultation with a gastroenterologist; AND
E) Dosage and administration are consistent with U.S. Food and Drug Administration approved label (i.e., 300 mg intravenous infusion every four weeks); AND
F) Provider attest to the absence of toxicity from natalizumab (such as as progressive multifocal leukoencephalopathy (PML) severe infections, etc.) as well as monitoring for JCV antibodies; AND
G) If patient began treatment while on chronic oral corticosteroids, the patient was able to be tapered off within 6 months of natalizumab initiation.

Initial Approval/ Extended Approval.
1 year (365 days)

Duration of Therapy in Tysabri. Indefinite.

Labs/Diagnostics. None required.

Waste Management for All Indications.
The dose in adults is 300 mg every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Tysabri has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes J2323

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HCPCS Code(s):	
J2323	Injection, natalizumab, 1 mg