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.

Criteria: CWQI HCS-0111

I. **Tysabri** is medically necessary as indicated by 1 or more of the following:

   a. **Multiple Sclerosis** with ALL of the following
      i. Patient is at least 18 years or older
      ii. Patient has diagnosis of relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) with relapses or progressive relapsing MS (PRMS)
      iii. Confirmed diagnosis of MS as documented by laboratory report (I.E. MRI)
      iv. Documented previous negative or unknown JCV antibody ELISA test within the past 6 months
      v. Prescriber and patient must be enrolled in and meet the conditions of the MS TOUCH program
      vi. Must be used as single agent therapy
      vii. Not used in combination with antineoplastic, immunosuppressant, or immunomodulating agents
      viii. Patient must not have a systemic medical condition resulting in significantly compromised immune system function
b. **Crohn’s disease** with **ALL** of the following
   i. Patient is at least 18 years or older
   ii. Patient has moderate to severe active disease
   iii. Documented trail 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
   iv. Documented trail and failure on **ONE** TNF-Inhibitor therapy for at least 3 months, unless contraindicated, such as Remicade (Infliximab), Cimzia (certolizumab) or Humira (adalimumab)
   v. Prescriber and patient must be enrolled in and meet the conditions of the CD TOUCH program
   vi. Used as single agent therapy [Not used concurrently with another TNF inhibitor or immunosuppressants (e.g. 6-mercaptopurine, azathioprine, cyclosporinemethotrexate, etc.)]
   vii. Documented previous negative or unknown JCV antibody ELISA test within the past 6 months
   viii. Prescriber and patient must be enrolled in and meet the conditions of the TOUCH program
   ix. Not used in combination with antineoplastic, immunosuppressant, or immunomodulating agents
   x. Patient must not have a systemic medical condition resulting in significantly compromised immune system function

c. **Renewal of Tysabri** is medically necessary as indicated by **ALL** of the following
   i. Patient continues to meet criteria above.
   ii. 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 intracelluar, bronchopulmonary aspergillosis, herpes, urinary tract, gastroenteritis, vaginal, tonsillitis) with **ONE** of the following:
   1. MS diagnosis with **ALL** of the following
      a. Adequate documentation of disease stability and/or improvement (i.e., EDSS scores, no relapse, and/or chart notes)
   2. Crohn’s Disease diagnosis with **ALL** of the following
      a. Clinical response and remission of disease is seen by 12 weeks
      b. Patient has been tapered off of oral corticosteroids within six months of starting Tysabri
      c. Patient does not require additional steroid use that exceeds three months in a calendar year to control their Crohn’s disease

d. **Contraindications/Warnings:**
   i. Tysabri increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability
ii. Patients should be monitored for signs and symptoms of PML and Tysabri discontinued immediately at the first sign or symptom suggesting PML.

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

iv. Tysabri is contraindicated in patients who have or have had PML

v. It is contraindicated in patient who had a hypersensitivity reaction to Tysabri.

**Dosage/Administration**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
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<tbody>
<tr>
<td>All Indications</td>
<td>300 mg intravenous infusion over one hour every four weeks</td>
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</tbody>
</table>

**Information to be Submitted with Pre-Authorization Request:**
1. Chart notes
2. Imaging studies and laboratory reports

**Applicable CPT Codes:**

**JCode:**
- J2323 – Tysabri (Elan Pharmaceuticals) 300mg injection: 1 billable unit = 1mg

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

**Dosing Limits:**

**Quantity Limit (max daily dose) [Pharmacy Benefit]:**
N/A

**Max Units (per dose and over time) [Medical Benefit]:**
- Male: 300 billable units every 28 days (4 weeks)
- Female: 300 billable units every 28 days (4 weeks)

**Covered Diagnosis:**

<table>
<thead>
<tr>
<th>ICD-10 Codes</th>
<th>Diagnosis</th>
</tr>
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<tbody>
<tr>
<td>G35</td>
<td>Multiple Sclerosis</td>
</tr>
<tr>
<td>K50.00</td>
<td>Crohn’s disease of small intestine without complication</td>
</tr>
<tr>
<td>K50.011</td>
<td>Crohn’s disease of small intestine with rectal bleeding</td>
</tr>
<tr>
<td>K50.012</td>
<td>Crohn’s disease of small intestine with intestinal obstruction</td>
</tr>
<tr>
<td>K50.013</td>
<td>Crohn’s disease of small intestine with fistula</td>
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</tbody>
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<tr>
<th>Reference</th>
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