Medical Pharmacy Drug Prior Authorization Criteria

Drug Trade Name:	Tysabri®, Tyruko®	**Drug Generic Name:**	Natalizumab
J Code:	J2323, Q5134	**1 billable unit =**	1 mg
Original Date of Review:	12/7/2022	**Last Reviewed:**	03/13/2024
Revision Date History	12/7/2022, 3/15/2023, 12/13/2023, 3/13/2024		

Natalizumab is a monoclonal antibody.

Criteria:

- **Length of authorization:**
  - **Crohn's Disease:**
    - Initial coverage will be provided for 6 months
    - Renewal coverage will be provided for up to 12 months
  - **Multiple Sclerosis:**
    - Initial coverage will be provided for 6 months
    - Renewal coverage will be provided for up to 12 months
- **Age:** see below for product specific requirements
- **Diagnoses [including ICD-10 codes]:** see below
- **Quantity Limit:**
  - Tysabri 300 mg/15 mL vial for injection: 1 vial per 28 days
  - Tyruko 300 mg/15 mL vial for injection: 1 vial per 28 days
- **Maximum Units:**

Indication	Billable Units	Per Number of Days
All	300	28

- **Initial Approval Criteria**
  - **Universal Criteria [if applicable]**
    - Patient is at least 18 years of age; **AND**
    - Prescriber and patient must be enrolled in and meet the conditions of the TOUCH program (Tysabri) or TYRUKO REMS program (Tyruko); **AND**
    - Documented negative JCV antibody ELISA test within the 6 months prior to therapy initiation; **AND**
    - Not used in combination with antineoplastic, immunosuppressant, or immunomodulating agents; **AND**
    - Patient must not have a systemic medical condition resulting in significantly compromised immune system function; **AND**
  - **Indication Specific Criteria [if applicable]**
    - **Multiple Sclerosis**
      - Patient has been diagnosed with a relapsing form of multiple sclerosis [i.e. relapsing- remitting disease (RRMS), active secondary progressive disease (SPMS), or clinically isolated syndrome (CIS)]; **AND**
      - Confirmed diagnosis of MS as documented by laboratory report (i.e. MRI); **AND**
      - 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; aminosalicylates may be continued during natalizumab therapy]

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)

Active secondary progressive MS (SPMS) is defined as the following:

• Expanded Disability Status Scale (EDSS) score ≥ 3.0; **AND**
• Disease is progressive ≥ 3 months following an initial relapsing-remitting course (i.e., EDSS score increase by 1.0 in patients with EDSS ≤5.5 or increase by 0.5 in patients with EDSS ≥6); **AND**
  ○ ≥ 1 relapse within the previous 2 years; **OR**
  ○ Patient has gadolinium-enhancing activity or new and unequivocally enlarging T2 contrast-enhancing lesions as evidenced by MRI

Definitive diagnosis of CIS is based upon ALL of the following:
• A monophasic clinical episode with patient-reported symptoms and objective findings reflecting a focal or multifocal inflammatory demyelinating event in the CNS • Neurologic symptom duration of at least 24 hours, with or without recovery • Absence of fever or infection • Patient is not known to have multiple sclerosis

Risk factors for the development of Progressive Multifocal Leukoencephalopathy (PML)
• Presence of anti-JCV antibodies. Patients who are anti-JCV antibody positive have a higher risk for developing PML. • Prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil) • Longer treatment duration, especially beyond 2 years • Elevated levels of anti-JCV antibody response index (i.e., index > 0.9). o 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.

Anti-JCV Antibody Negative	Natalizumab Exposure (months)	Anti-JCV Antibody Positive	
		No Prior Immunosuppressant Use	Prior Immunosuppressant Use
1/10,000	1-24	<1/1,000	1/1,000
	25-48	2/1,000	6/1,000
	49-72	4/1,000	7/1,000
	73-96	2/1,000	6/1,000

Note: Requirements for JCV negativity are based upon recommendations from current guidelines. Use in patients who are anti-JCV antibody positive will be reviewed on a case-by-case basis.

- **Renewal Criteria**
  - Coverage can be renewed based upon the following criteria:
    - Patient continues to meet the universal and other indication-specific relevant criteria identified in initial approval criteria; **AND**
    - Absence of unacceptable toxicity from the drug
      - Examples of unacceptable toxicity include: hypersensitivity reactions/antibody formation, hepatotoxicity, signs or symptoms of progressive multifocal leukoencephalopathy (PML), herpes infections (including herpes encephalitis and meningitis and acute retinal necrosis), immunosuppression, infections (including pneumonias, pneumocystis carinii pneumonia, pulmonary mycobacterium avium intracellulare, bronchopulmonary aspergillosis, herpes, urinary tract infections, gastroenteritis, vaginal infections, tooth infections, tonsillitis, etc.), thrombocytopenia, etc.; **AND**

  - **Multiple Sclerosis**
    - Continuous monitoring of response to therapy indicates a beneficial response* [manifestations of increased 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)]

*Note:

- 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 oral corticosteroids within six months of starting natalizumab; **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.]

- **Dosage/Administration**

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

HCPCS Code:

- J2323 - Injection, natalizumab, excludes biosimilar, (Tysabri), 1 mg; 1 billable unit = 1 mg
- Q5134 - Injection, natalizumab-sztn, biosimilar, (Tyruko), 1 mg; 1 billable unit = 1 mg

NDC:

- Tysabri 300 mg/15 mL single-use vial: 64406-0008-xx
- Tyruko 300 mg/15 mL single-use vial: 61314-0543-xx

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

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