Natalizumab Products (Tysabri, Tyruko)

When requesting a natalizumab product, the individual requiring treatment must be diagnosed with one of the following FDA-approved indications and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

FDA-approved Indications

Multiple Sclerosis (MS)
Natalizumab indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Crohn's Disease (CD)
Natalizumab is indicated 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.

Coverage Guidelines

Multiple Sclerosis (MS)

The individual must meet **all** of the following criteria for initial authorization:

- Has a relapsing form of multiple sclerosis (i.e., clinically isolated syndrome, relapsing-remitting disease, or active secondary progressive MS);
- Is 18 years of age or older;
- Prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis;
- Meets one of the following:
    - Has experienced inadequate efficacy or significant intolerance to at least one disease-modifying agent used for MS (e.g., Aubagio, Avonex, Bafiertam, Betaseron, Briumvi, Copaxone, Extavia , Gilenya, Glatopa, Kesimpta, Lemtrada, Mavenclad, Mayzent, Ocrevus, Ocrevus Zunovo, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Vumerity, or Zeposia); OR
    - Has highly-active or aggressive multiple sclerosis defined as one of the following:
        - Has demonstrated rapidly-advancing deterioration(s) in physical functioning (e.g., loss of mobility/or lower levels of ambulation, severe changes in strength or coordination); OR
        - Disabling relapse(s) with suboptimal response to systemic corticosteroids; OR

- Magnetic resonance imaging [MRI] findings suggest highly-active or aggressive multiple sclerosis (e.g., new, enlarging, or a high burden of T2 lesions or gadolinium-enhancing lesions); OR
- Manifestations of multiple sclerosis-related cognitive impairment.

The individual must meet **all** of the following criteria for reauthorization:
- Is 18 years of age or older;
- Has relapsing form of multiple sclerosis (i.e., clinically isolated syndrome, relapsing-remitting disease, or active secondary progressive disease);
- Prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis;
- For an individual who has received a natalizumab product for at least one year, must meet one of the following:
    - Has experienced a beneficial clinical response by at least one objective measure (e.g., stabilization or reduced worsening in disease activity as evaluated by magnetic resonance imaging [MRI], stabilization or reduced worsening on the Expanded Disability Status Scale [EDSS] score, achievement in criteria for No Evidence of Disease Activity-3 [NEDA-3] or NEDA-4, improvement on the fatigue symptom and impact questionnaire-relapsing multiple sclerosis [FSIQ-RMS] scale, reduction or absence of relapses, improvement or maintenance on the six-minute walk test or 12-Item Multiple Sclerosis Walking Scale, improvement on the Multiple Sclerosis Functional Composite [MSFC] score, and/or attenuation of brain volume loss); OR
    - Has experienced stabilization, slowed progression, or improvement in at least one symptom (e.g., motor function, fatigue, vision, bowel/bladder function, spasticity, walking/gait, or pain/numbness/tingling sensation).

Crohn's disease (CD)

The individual must meet **all** of the following criteria for initial authorization:
- Has moderately to severely active Crohn's disease;
- Is 18 years of age or older;
- Prescribed by or in consultation with a gastroenterologist;
- Has tried at least two biologics for Crohn's disease (e.g., an adalimumab product, Cimzia, an infliximab intravenous product, Entyvio, Skyrizi, or Stelara).
  (Note: Each biosimilar tried from the same chemical would only count as a trial of one product.)

The individual must meet **all** of the following criteria for reauthorization:
- Has been established on a natalazimab product for at least 6 months;
  (Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criteria for initial therapy.)
- Is 18 years of age or older;
- Prescribed by or in consultation with a gastroenterologist;
- Meets one of the following:

- Has experienced a beneficial clinical response from baseline by at least one objective measure (e.g., fecal markers, serum markers, imaging studies, endoscopic assessment, and/or reduced dose of corticosteroids); OR
- Has experienced an improvement in at least one symptom (e.g., decreased pain, fatigue, stool frequency, and/or blood in stool).

Approval Duration:
MS (initial and reauthorization): 12 months
CD initial: 6 months; reauthorization: 12 months

Dosing Recommendation

The recommended dose of natalizumab is 300 mg intravenous infusion over one hour every 4 weeks.

References

1. Tysabri® intravenous infusion [prescribing information]. Cambridge, MA: Biogen; March 2025.
2. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. Updated September 2019.
3. McGinley MP, Goldschmidt C, Rae-Grant AD. Diagnosis and treatment of multiple sclerosis. A review. *JAMA*. 2021;325(8):765-779.
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5. Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*. 2014;83:278-286.
6. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018;17(2):162-173.
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8. Gordon FH, Hamilton MI, Donoghue S, et al. A pilot study of treatment of active ulcerative colitis with natalizumab, a humanized monoclonal antibody to alpha-4 integrin. *Aliment Pharmacol Ther*. 2002;16:699-705.
9. Tyruko® intravenous infusion [prescribing information]. Princeton, NJ: Sandoz; August 2023.
10. Dolinger M, Torres J, Vermeire S. Crohn's disease. *Lancet*. 2024;403(10432):1177-1191.