natalizumab

Commercial Medical Benefit Drug Policy

natalizumab (Tysabri)
natalizumab-sztn (Tyruko)

Drug Details

USP Category: CENTRAL NERVOUS SYSTEM AGENTS

Mechanism of Action: recombinant humanized anti-α4-integrin monoclonal antibody

HCPCS:
J2323:Injection, natalizumab, 1 mg
Q5134:Injection, natalizumab-sztn (tyruko), biosimilar, 1 mg

How Supplied:
300 mg (Solution for dilution prior to infusion)

Condition(s) listed in policy *(see coverage criteria for details)*

- Crohn's Disease, moderate to severe
- Multiple Sclerosis, relapsing (RMS)

Any condition not listed in this policy requires a review to confirm it is medically necessary. For conditions that have not been approved for intended use by the Food and Drug Administration (i.e., off-label use), the criteria outlined in the Health and Safety Code section 1367.21 must be met.

Special Instructions and Pertinent Information

Provider must submit documentation (such as office chart notes, lab results or other clinical information) to ensure the member has met all medical necessity requirements.

The member's specific benefit may impact drug coverage. Other utilization management processes, and/or legal restrictions may take precedence over the application of this clinical criteria.

For billing purposes, drugs must be submitted with the drug's assigned HCPCS code (as listed in the drug policy) and the corresponding NDC (national drug code). An unlisted, unspecified, or miscellaneous code should not be used if there is a specific code assigned to the drug.

Members with the following plans: **PPO, Direct Contract HMO, and when applicable, ASO, Shared Advantage, HMO (non-direct)** may be required to have their medication administered at a preferred site of service, including the home, a physician's office, or an independent infusion center not associated with a hospital.

For members that cannot receive infusions in the preferred home or ambulatory setting AND meet one of the following criteria points, drug administration may be performed at a hospital outpatient facility infusion center.

CRITERIA FOR HOSPITAL OUTPATIENT FACILITY ADMINISTRATION

MCG Care Guidelines, 19th edition, 2015

ADMINISTRATION OF THIS DRUG IN THE HOSPITAL OUTPATIENT FACILITY SITE OF CARE REQUIRES ONE OF THE FOLLOWING: (*Supporting Documentation must be submitted)*

1. Patient is receiving their first infusion of natalizumab or is being re-initiated on natalizumab after at least 6 months off therapy. *Subsequent doses will require medical necessity for continued use in the hospital outpatient facility site of care.*

OR

Additional clinical monitoring is required during administration as evidenced by one of the following:

2. Patient has experienced a previous severe adverse event on natalizumab based on documentation submitted.
3. Patient continues to experience moderate to severe adverse events on natalizumab based on documentation submitted, despite receiving premedication such as acetaminophen, steroids, diphenhydramine, fluids, etc.
4. Patient is clinically unstable based on documentation submitted.
5. Patient is physically or cognitively unstable based on documentation submitted.

Coverage Criteria
The following condition(s) require Prior Authorization/Preservice.

Crohn's Disease, moderate to severe

Meets medical necessity if all the following are met:

Initial:

1. ***Effective 2/1/2026 and after***: Prescribed by or in consultation with a gastroenterologist
2. Not taking in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, methotrexate, cyclosporine), a TNF-α inhibitor or anakinra (Kineret)
3. Inadequate response or intolerable side effect to two preferred agents (e.g., adalimumab-aacf, infliximab (Avsola or Inflectra), Rinvoq, Skyrizi, Yesintek), or contraindication to all preferred agents

Reauthorization:

1. Patient is responding to therapy
2. ***Effective 2/1/2026 and after***: Not being used in combination with an immunosuppressant (e.g. azathioprine, 6-mercaptopurine, methotrexate, cyclosporine, TNF inhibitor, or Kineret (anakinra))

Covered Doses:
Up to 300 mg given intravenously every 4 weeks

Coverage Period:
Yearly

ICD-10:
K50.00-K50.119, K50.80-K50.919

Multiple Sclerosis, relapsing (RMS)
Meets medical necessity if all the following are met:
Initial
1. Inadequate response or intolerance to at least one generic agent (e.g., fingolimod, dimethyl fumarate, glatiramer, Glatopa), or contraindication to all generic agents
2. Not being used in combination with another disease-modifying therapy for multiple sclerosis (e.g., Aubagio, Avonex, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Rebif, Tecfidera, mitoxantrone, Ocrevus)

Reauthorization
1. Patient is responding to therapy
2. ***Effective 2/1/2026 and after***: Not being used in combination with another disease-modifying therapy for multiple sclerosis (e.g. Aubagio, Avonex, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Rebif, Tecfidera, mitoxantrone, Ocrevus)

Covered Doses:
Up to 300 mg given intravenously every 4 weeks

Coverage Period:
Yearly

ICD-10:
G35

References

1. AHFS. Available by subscription at http://www.lexi.com
2. DrugDex. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
3. Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018 Apr;113(4):481-517.
4. Havrdova E, Galetta S, Hutchinson M, et al. Effect of natalizumab on clinical and radiological disease activity in multiple sclerosis: a retrospective analysis of the Natalizumab Safety and Efficacy in Relapsing-Remitting Multiple Sclerosis (AFFIRM) study. Lancet Neurol. 2009 Mar;8(3):254-60.
5. Hutchinson M, Kappos L, Calabresi PA, et al. The efficacy of natalizumab in patients with relapsing multiple sclerosis: subgroup analyses of AFFIRM and SENTINEL. J Neurol. 2009 Mar;256(3):405-15.
6. MCG Care Guidelines, 19th edition, 2015, Home Infusion Therapy, CMT: CMT-0009(SR)
7. Rae-grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018;90(17):777-788. [Guideline reaffirmed October 19, 2024].
8. Terdiman JP, Gruss CB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute guideline on the use of thiopurines, methotrexate, and anti-TNF-alpha biologic drugs

for the induction and maintenance of remission in inflammatory Crohn's disease. Gastroenterology 2013; 145:1459-63.
9. Tyruko (natalizumab-sztn) Prescribing Information. Sandoz Inc., Princeton, NJ. 8/2023.
10. Tysabri (natalizumab) [prescribing information]. Cambridge, MA: Biogen Inc; 3/2025.

Review History

Date of Last Annual Review: 4Q2025
Changes from previous policy version:

- Added new biosimilar Tyruko
- Multiple sclerosis: ***Effective 2/1/2026 and after***, will update reauthorization criteria (Rationale: Ensure appropriate use)
- Crohn's disease: ***Effective 2/1/2026 and after***, will add prescriber specialty and update reauthorization criteria (Rationale: Ensure appropriate use)

Blue Shield of California Medication Policy to Determine Medical Necessity
Reviewed by P&T Committee