RX.PA.036.MPC NATALIZUMAB PRODUCTS (Tysabri®, Tyruko®)

The purpose of this policy is to define the prior authorization process for Tysabri® (natalizumab) and Tyruko® (natalizumab-sztn).

Tysabri® (natalizumab) and Tyruko® (natalizumab-sztn) is indicated as monotherapy for the treatment of members with relapsing forms of multiple sclerosis (MS) and for inducing and maintaining clinical response and remission in patients with moderately to severely active Crohn's disease (CD) with evidence of inflammation, who had an inadequate response to, or are unable to tolerate conventional CD therapies and Tumor Necrosis Factor (TNF) alpha inhibitors.

DEFINITIONS

Kurtzke Expanded Disability Status Scale (EDSS) – a method of quantifying disability in multiple sclerosis (MS). EDSS steps 1.0 to 4.5 refer to MS patients who are fully ambulatory; EDSS steps 5.0 to 9.5 are defined by the impairment in ambulation.

Tysabri Outreach Unified: Commitment to Health (TOUCH™) – TOUCH is a restricted distribution program focused on safety and developed with the help of the FDA. Only prescribers and patients enrolled in the TOUCH prescribing program can prescribe and receive Tysabri® (natalizumab) and only certain pharmacies and infusion sites authorized by the TOUCH prescribing program can dispense and infuse Tysabri® (natalizumab).

PROCEDURE

A. Initial Authorization Criteria:

Must meet all of the criteria listed under the respective diagnosis:

For All Diagnoses:

- Requests for Tysabri® (natalizumab) and Tyruko® (natalizumab-sztn) are subject to the preferred medical medication list.

	Products
Preferred	• **Tyruko® (natalizumab-sztn)**
Non-preferred	• **Tysabri® (natalizumab)**

1. Multiple Sclerosis

- Must be prescribed by a neurologist who is registered with the REMS prescribing program

- Must have a diagnosis of a relapsing form of MS
- Must be age 18 years or older
- Must have a John Cunningham virus (JCV) antibody test completed within 3 months and provider attests that risks/benefits of treatment have been discussed
- Must have previously had an inadequate response or intolerance to the following multiple sclerosis therapies: Fingolimod (Gilenya) and Dimethyl fumarate (Tecfidera)
- Must currently not have or have a history of progressive multifocal leukoencephalopathy (PML)
- Must not be receiving chronic immunosuppressant or immunomodulatory therapy (including interferon beta-1a, interferon beta-1b, glatiramer acetate, or fingolimod) or have systemic medical conditions resulting in significant compromised immune system function

2. Crohn's Disease

- Must be prescribed by a gastroenterologist who is registered with the REMS prescribing program
- Must have a diagnosis of moderately to severely active CD with inflammation
- Must be age 18 years or older
- Must have a John Cunningham virus (JCV) antibody test completed within 3 months and provider attests that risks/benefits of treatment have been discussed
- Must have previously tried conventional therapies such as 3 months of immunomodulators (i.e., azathioprine, 6-mercaptopurine) or had an inadequate response or intolerance, side effects/toxicity, or have a contraindication to at least 2 of these therapies
- Must have an adequate trial of at least 3 months with a preferred adalimumab product with an inadequate response, significant side effects/toxicity, or have a contraindication to this therapy
- Must not currently have or have a history of progressive multifocal leukoencephalopathy (PML)
- Must not be receiving concomitant chronic immunosuppressant or immunomodulatory therapy (including 6-mercaptopurine, azathioprine, cyclosporine, methotrexate, or inhibitors of TNF-alpha) or have systemic medical conditions resulting in significant compromised immune system function
  Note: If Member is taking corticosteroids, they must be tapered off within 6 months of initiating natalizumab products

B. Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc) listed in the FDA approved labeling.

C. Natalizumab products will be considered investigational or experimental for any other use and will not be covered.

D. Reauthorization Criteria:

	Products
Preferred	• **Tyruko® (natalizumab-sztn)**
Non-preferred	• **Tysabri® (natalizumab)**

All prior authorization renewals are reviewed to determine the Medical Necessity for continuation of therapy. Authorization may be extended based upon:

1. Multiple Sclerosis:

- MPC Renewal:
  - Chart documentation from the provider that the member's condition has stabilized or improved based upon the prescriber's assessment while on therapy
  - Documentation that there is no evidence of progressive multifocal leukoencephalopathy (PML)
  - Member must continue to be enrolled in the REMS prescribing program
- Renewal from Previous Insurer:
  - Members who have received prior approval (from insurer other than MPC), or have been receiving medication samples, should be considered under criterion A.1 (Initial Authorization Criteria, Multiple Sclerosis).
  - Provider has a documented clinical response of the member's condition which has stabilized or improved based upon the prescriber's assessment.

2. Crohn's Disease:

- MPC Renewal:
  - Started a natalizumab product while NOT on chronic oral corticosteroids: chart documentation from the provider that the member's condition has stabilized or improved based upon the prescriber's assessment while on therapy
  - Started a natalizumab product while on chronic oral corticosteroids: the patient is tapered off oral corticosteroids within 6 months of starting Tysabri®
  - For all Crohn's disease patients, must have documentation that there is no evidence of progressive multifocal leukoencephalopathy (PML)
  - Member must continue to be enrolled in the REMS prescribing program
- Renewal from Previous Insurer:
  - Members who have received prior approval (from insurer

other than MPC), or have been receiving medication samples, should be considered under criterion A.2 (Initial Authorization Criteria, Crohn's Disease).

- Provider has a documented clinical response of the member's condition which has stabilized or improved based upon the prescriber's assessment.

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	• Multiple Sclerosis: Up to 1 year • Crohn's Disease (Not on chronic oral corticosteroids): up to 3 months • Crohn's Disease (On chronic oral corticosteroids): up to 6 months
Reauthorization	Up to 1 year
Quantity Level Limit	
Natalizumab products	1 vial per 28 days

Codes: J Code(s)

Code	Description
J2323	Injection, natalizumab, 1 mg
Q5134	Injection, natalizumab-sztyn (Tyruko), biosimilar, 1mg

REFERENCES

1. Tysabri [package insert]. Cambridge, MA: Biogen Idec Inc.; January 2008.
2. Yousry T, Habil M, Major E, et al. Evaluation of Patients Treated with Natalizumab for Progressive Multifocal Leukoencephalopathy. N Engl J Med 2006;354:924-933.
3. Rudick R, Stuart W, Calabresi P, et al. Natalizumab plus Interferon Beta-1a for Relapsing Multiple Sclerosis. N Engl J Med 2006;354:911-923.
4. Polman C, O'Connor P, Havrdova E, et al. A Randomized, Placebo-Controlled Trial of Natalizumab for Relapsing Multiple Sclerosis. N Engl J Med 2006;354:899-910.
5. American Gastroenterological Association Institute Technical Review on Corticosteroids, Immunomodulators, and Infliximab in Inflammatory Bowel Disease. Gastroenterology 2006; 130:940-987.
6. Lichtenstein GR, Hanauer SB et al. American College of Gastroenterology Practice Guidelines on the Management of Crohn's Disease in Adults. Am J Gastroenterol 2009; 1-19.
7. 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;256:405-415
8. Coyle PK, Foley JF, Fox EJ, et al. Best practice recommendations for the selection and management of patients with multiple sclerosis receiving natalizumab therapy. Mult Scler 2009:15:S26
9. Kappos L, Bates D, Hartung H, et al. Natalizumab treatment for multiple sclerosis: recommendations for patient selection and monitoring. Lancet Neurol 2007;6:431-41.
10. 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;8:254-60.

REVIEW HISTORY

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Update to include the preferred vs non-preferred product list under the continuation of therapy pathway	*09/2026*
Update to clarify treatment requirements under MS, preferred vs non-preferred status with biosimilar – Tyruko and update to include HCPCS for Tyruko	*04/2026*
Annual Review	*02/2026*
Annual Review	*02/2025*
Annual Review *Change in Non-MPC renewal to renewal from previous insurer*	*02/2024*
Annual review	*02/2023*
Selected Revision *Addition of MPC vs Non-MPC Renewal Criteria*	*08/2022*
Annual review	*02/2022*
Addition of dosing requirements and off-label restrictions	*12/2021*
P&T Review	*11/2020*