Natalizumab (Tyruko® & Tysabri®)

Policy Number: 2026D0026T
Effective Date: July 1, 2026

➲ Instructions for Use

Table of Contents **Page**

Coverage Rationale 1
Applicable Codes 2
Background 3
Benefit Considerations 3
Clinical Evidence 4
U.S. Food and Drug Administration 6
Centers for Medicare and Medicaid Services 6
References 6
Policy History/Revision Information 7
Instructions for Use 7

Community Plan Policy

- Natalizumab (Tyruko® & Tysabri®)

Coverage Rationale

➲ See Benefit Considerations

This policy refers to the following natalizumab products for injection:

- Tyruko (natalizumab-sztn)
- Tysabri (natalizumab)
- Any FDA-approved natalizumab biosimilar product not listed here*

*Any U.S. Food and Drug Administration approved and launched natalizumab biosimilar product not listed by name in this policy will be considered non-preferred until reviewed by UnitedHealthcare.

Diagnosis-Specific Criteria

"Natalizumab" will be used to refer to all natalizumab products.

Natalizumab is proven for the treatment of:

- **Relapsing forms of Multiple Sclerosis**
  Natalizumab is medically necessary for the treatment of relapsing forms of multiple sclerosis (MS) when all of the following are met:
  - Initial Therapy
    - Diagnosis of relapsing forms of multiple sclerosis (MS) (e.g., clinically isolated syndrome, relapsing-remitting disease, active secondary-progressive disease); **and**
    - Patient is **not** receiving natalizumab in combination with **any** of the following (used as monotherapy):
      – Disease modifying therapy (e.g., interferon beta preparations, glatiramer acetate, fingolimod, cladribine, siponimod, or teriflunomide)
      – B cell targeted therapy (e.g., rituximab, belimumab, ofatumumab)
      – Lymphocyte trafficking blockers (e.g., alemtuzumab, mitoxantrone)
      and
    - Natalizumab is dosed according to the U.S. FDA labeled dosing; **and**
    - Initial authorization is for no more than 12 months
  - Continuation of Therapy
    - Patient has previously received treatment with natalizumab; **and**
    - Documentation of positive clinical response to natalizumab therapy; **and**
    - Patient is **not** receiving natalizumab in combination with **any** of the following (used as monotherapy):

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

- Disease modifying therapy (e.g., interferon beta preparations, glatiramer acetate, fingolimod, cladribine, siponimod, or teriflunomide)
- B cell targeted therapy (e.g., rituximab, belimumab, ofatumumab)
- Lymphocyte trafficking blockers (e.g., alemtuzumab, mitoxantrone)

and

- Natalizumab is dosed according to the U.S. FDA labeled dosing; **and**
- Authorization is for no more than 12 months

- **Crohn's Disease**
  Natalizumab is medically necessary for inducing and maintaining clinical response and remission in patients with moderate to severe Crohn's disease (CD) when all of the following are met:
  - Initial Therapy
    - Diagnosis of moderately to severely active Crohn's disease; **and**
    - History of inadequate response or intolerance to conventional Crohn's disease therapies and inhibitors of TNF-α. Conventional Crohn's disease therapies may include aminosalicylates (such as mesalamine and sulfasalazine), corticosteroids, immunomodulators (such as azathioprine, 6-mercaptopurine, and methotrexate) and TNF-inhibitors [e.g., infliximab, adalimumab, certolizumab pegol (Cimzia®)]; **and**
    - Patient is not receiving concomitant treatment with immunosuppressants (e.g., 6-MP, azathioprine, cyclosporine, or methotrexate) **or** TNF-inhibitors [e.g., Enbrel (etanercept), infliximab, adalimumab, or certolizumab pegol (Cimzia)]; **and**
    - Natalizumab is dosed according to the U.S. FDA labeled dosing; **and**
    - Initial authorization is for no more than 12 months
  - Continuation of Therapy
    - Patient has previously received treatment with natalizumab; **and**
    - Documentation of positive clinical response to natalizumab therapy; **and**
    - Patient is not receiving concomitant treatment with immunosuppressants (e.g., 6-MP, azathioprine, cyclosporine, or methotrexate) or TNF-inhibitors [e.g., Enbrel (etanercept), adalimumab, certolizumab pegol (Cimzia), or infliximab]; **and**
    - Natalizumab is dosed according to the U.S. FDA labeled dosing; **and**
    - Authorization is for no more than 12 months

Natalizumab is unproven for the treatment of other conditions or diseases, including types of MS other than relapsing forms. Statistically robust randomized controlled trials are needed to address the issue of whether natalizumab has sufficient superiority in clinical efficacy compared to other available treatments to justify the substantial inherent clinical risk in its use.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other policies and guidelines may apply.

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

Diagnosis Code	Description
G35.A	Relapsing-remitting multiple sclerosis
G35.B0	Primary progressive multiple sclerosis, unspecified
G35.B1	Active primary progressive multiple sclerosis
G35.B2	Non-active primary progressive multiple sclerosis
G35.C0	Secondary progressive multiple sclerosis, unspecified
G35.C1	Active secondary progressive multiple sclerosis
G35.C2	Non-active secondary progressive multiple sclerosis
G35.D	Multiple sclerosis, unspecified

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Diagnosis Code	Description
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

Background

Natalizumab is a recombinant humanized IgG4κ monoclonal antibody produced in murine myeloma cells. Natalizumab binds to the α4-subunit of α4β1 and α4β7 integrins expressed on the surface of all leukocytes except neutrophils and inhibits the α4-mediated adhesion of leukocytes to their counter-receptor(s). The receptors for the α4 family of integrins include vascular cell adhesion molecule-1 (VCAM-1), which is expressed on activated vascular endothelium, and mucosal addressing cell adhesion molecule-1 (MAdCAM-1) present on vascular endothelial cells of the gastrointestinal tract. Disruption of these molecular interactions prevents transmigration of leukocytes across the endothelium into inflamed parenchymal tissue. The specific mechanism(s) by which natalizumab exerts its effects in multiple sclerosis and Crohn's disease have not been fully defined.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Proven

Relapsing Multiple Sclerosis

O'Connor et al conducted a prospective, observational, open-label Safety of Tysabri Re-dosing and Treatment (STRATA) Study which evaluated long-term safety and efficacy of patients (n = 1,094) treated with natalizumab over 240 weeks.[7] Patients previously enrolled in relapsing-remitting multiple sclerosis (RRMS) natalizumab clinical trials that received natalizumab 300 mg IV every 4 weeks were included. Researchers reported that serious adverse events (including progressive multifocal leukoencephalopathy) were consistent with natalizumab's known safety profile; short exposure with a gap before redosing was associated with higher incidences of anti-natalizumab antibodies and hypersensitivity reactions. Stability of EDSS scores and consistently low relapse rates over 5 years of natalizumab treatment were with its known efficacy profile. Patients originally randomized to placebo/another disease-modifying therapy vs natalizumab in previous studies had significantly higher EDSS scores at STRATA baseline; this difference persisted over 240 weeks. Researchers concluded that this study provided Class III evidence that RRMS patients treated with natalizumab experienced stabilized EDSS scores, decreased relapse rates, and is associated with an increased risk of progressive multifocal leukoencephalopathy.

The Tysabri (natalizumab) Observational Program (TOP) was an open-label, multinational, 10-year prospective study in clinical practice settings which evaluated the safety and efficacy of natalizumab therapy in patients (n = 4821) with relapsing-remitting multiple sclerosis (RRMS). Results of the 5-year interim analysis showed that there were no new safety signals. There were 18 cases of progressive multifocal leucoencephalopathy reported, following 11-44 natalizumab infusions. The mean annualized relapse rate decreased from 1.99 in the 12 months prior to baseline to 0.31 on natalizumab therapy ($p < 0.0001$), remaining low at 5 years. Lower annualized relapse rates were observed in patients who used natalizumab as first MS therapy, in patients with lower baseline EDSS scores, and in patients with lower pre-natalizumab relapse rates. Mean EDSS scores remained unchanged up to 5 years. Researchers concluded that this interim analysis confirmed natalizumab's overall safety profile and the low relapse rate and stabilized disability levels in natalizumab-treated patients with RRMS in clinical practice.

A Cochrane systemic review in 2015 compared the benefit and acceptability of interferon beta-1b, interferon beta-1a (Avonex, Rebif), glatiramer acetate, natalizumab, mitoxantrone, fingolimod, teriflunomide, dimethyl fumarate, alemtuzumab, pegylated interferon beta-1a, daclizumab, laquinimod, azathioprine and immunoglobulins for the treatment of people with relapsing-remitting multiple sclerosis (RRMS) and to provide a ranking of these treatments according to their benefit and acceptability, defined as the proportion of participants who withdrew due to any adverse event. The authors included randomized controlled trials (RCTs) that studied one or more of the 15 treatments as monotherapy, compared to placebo or to another active agent, for use in adults with relapsing-remitting multiple sclerosis (RRMS) were included. The authors included 39 studies in this review, in which 25,113 participants were randomized. The majority of the included trials were short-term studies, with a median duration of 24 months. Twenty-four (60%) were placebo-controlled and 15 (40%) were head-to-head studies. Network meta-analysis showed that, in terms of a protective effect against the recurrence of relapses in RRMS during the first 24 months of treatment, alemtuzumab, mitoxantrone, natalizumab, and fingolimod outperformed other drugs. The most effective drug was alemtuzumab (risk ratio (RR) versus placebo 0.46, 95% confidence interval (CI) 0.38 to 0.55; surface under the cumulative ranking curve (SUCRA) 96%; moderate quality evidence), followed by mitoxantrone (RR 0.47, 95% CI 0.27 to 0.81; SUCRA 92%; very low quality evidence), natalizumab (RR 0.56, 95% CI 0.47 to 0.66; SUCRA 88%; high quality evidence), and fingolimod (RR 0.72, 95% CI 0.64 to 0.81; SUCRA 71%; moderate quality evidence). Disability worsening was based on a surrogate marker, defined as irreversible worsening confirmed at three-month follow-up, measured during the first 24 months in the majority of included studies. Both direct and indirect comparisons revealed that the most effective treatments were mitoxantrone (RR versus placebo 0.20, 95% CI 0.05 to 0.84; SUCRA 96%; low quality evidence), alemtuzumab (RR 0.35, 95% CI 0.26 to 0.48; SUCRA 94%; low quality evidence), and natalizumab (RR 0.64, 95% CI 0.49 to 0.85; SUCRA 74%; moderate quality evidence). Almost all of the agents included in this review were associated with a higher proportion of participants who withdrew due to any adverse event compared to placebo. Based on the network meta-analysis methodology, the corresponding RR estimates versus placebo over the first 24 months of follow-up were: mitoxantrone 9.92 (95% CI 0.54 to 168.84), fingolimod 1.69 (95% CI 1.32 to 2.17), natalizumab 1.53 (95% CI 0.93 to 2.53), and alemtuzumab 0.72 (95% CI 0.32 to 1.61). The authors state that alemtuzumab, natalizumab, and fingolimod are the best choices for preventing clinical relapses in people with RRMS, but this evidence is limited to the first 24 months of follow-up. For the prevention of disability worsening in the short term (24 months), only natalizumab shows a beneficial effect on the basis of moderate quality evidence (all of the other estimates were based on low to very low-quality evidence). Currently, therefore, insufficient evidence is available to evaluate treatments for the prevention of irreversible disability worsening.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Crohn's Disease

A 2018 update of the 2015 Cochrane systemic review summarizes the current evidence on the use of natalizumab for induction of remission in Crohn's disease (CD). The authors included five randomized controlled trials (RCTs) comparing natalizumab to a placebo or control therapy for induction of remission in CD. A total of five RCTs (1771 participants) were included. Four studies (1692 participants) compared one, two or three infusions of natalizumab (300 mg or 3 mg/kg or 6mg/kg) to placebo. One study (79 participants) compared three infusions of natalizumab (300 mg) and infliximab (5 mg/kg) to infliximab and placebo. Four studies were rated as low risk of bias. One study was rated as unclear risk of bias for selective reporting. One, two and three infusions of natalizumab were superior to placebo for induction of remission and clinical response. Infusions were administered at weeks zero, four and eight. After one infusion, 76% (849/1117) of natalizumab participants failed to enter remission at 4 weeks compared to 83% (411/494) of placebo participants (RR 0.91, 95% CI 0.86 to 0.96, 3 studies, GRADE high quality). At 4 weeks, the RR for clinical response was 0.78 (95% CI 0.66 to 0.92, 3 studies, 1611 participants, GRADE moderate quality). After two infusions, after 8 weeks, 66% (693/1049) of natalizumab participants failed to enter remission compared to 77% (382/494) of placebo participants (RR 0.85, 95% CI 0.76 to 0.95; 3 studies, GRADE moderate quality). At 8 weeks, the RR for clinical response was 0.73 (95% CI 0.58 to 0.91, 3 studies, 1543 participants, GRADE low quality). After three infusions, at 12 weeks, 61% (596/983) of natalizumab participants failed to enter remission compared to 73% (313/431) of placebo participants (RR 0.85, 95% CI 0.78 to 0.92, 2 studies, GRADE high quality). At 12 weeks, the RR for clinical response was 0.76 (95% CI 0.67 to 0.86, 2 studies, 1414 participants, GRADE high quality). One study (507 participants) reported on change in CDAI from baseline. Natalizumab participants had a larger drop in mean CDAI scores than placebo participants at 4, 8, and 12 weeks. The study comparing combination therapy with natalizumab and infliximab to infliximab and placebo demonstrated similar remission rates at 10 weeks. Sixty-four per cent (33/52) of participants assigned to natalizumab and infliximab failed to achieve remission compared to 70% (19/27) assigned to placebo and infliximab (RR 0.90, 95% CI 0.65 to 1.24, GRADE moderate quality). Natalizumab is associated with the development of progressive multifocal leukoencephalopathy (PML) resulting in some patient deaths. There are currently no tests which can reliably predict those at risk of developing PML. The authors concluded that high quality data suggest that natalizumab is effective for induction of clinical remission and response in some patients with moderately to severely active CD. However, none of the included studies had the power to detect rare but serious adverse events such as PML. Due to the association with PML, and the availability of alternative agents that are not associated with PML, natalizumab is not likely to be used in patients who fail currently available medical therapy. The use of natalizumab in select patients (e.g., patients allergic to different biologics) needs to be carefully considered against the potential risk of developing PML. Further studies of natalizumab are not likely to be done.

Professional Societies

American Academy of Neurology

In 2018, the American Academy of Neurology developed recommendations for disease-modifying therapy (DMT) for multiple sclerosis (MS). Thirty recommendations were developed. The following recommendations applied to natalizumab:

- Clinicians should prescribe alemtuzumab, fingolimod, or natalizumab for people with MS with highly active MS (Level B).
- Clinicians may initiate natalizumab treatment in people with MS with positive anti-JCV antibody indexes above 0.9 only when there is a reasonable chance of benefit compared with the low but serious risk of PML (Level C).
- Clinicians should evaluate the degree of disease activity, adherence, AE profiles, and mechanism of action of DMTs when switching DMTs in people with MS with breakthrough disease activity during DMT use (Level B).
- Clinicians should counsel people with MS considering natalizumab, fingolimod, rituximab, ocrelizumab, and dimethyl fumarate about the PML risk associated with these agents (Level B).
- Clinicians should discuss switching to a DMT with a lower PML risk with people with MS taking natalizumab who are or become JCV antibody–positive, especially with an index of above 0.9 while on therapy (Level B).
- Clinicians should counsel that new DMTs without long-term safety data have an undefined risk of malignancy and infection for people with MS starting or using new DMTs (Level B).
- People with MS with serious infections potentially linked to their DMT should switch DMTs (does not pertain to PML management in people with MS using DMT) (Level B).
- Clinicians should check for natalizumab antibodies in people with MS who have infusion reactions before subsequent infusions, or in people with MS who experience breakthrough disease activity with natalizumab use (Level B).
- Clinicians should switch DMTs in people with MS who have persistent natalizumab antibodies (Level B).
- Physicians must counsel people with MS considering natalizumab discontinuation that there is an increased risk of MS relapse or MRI-detected disease activity within 6 months of discontinuation (Level A).
- Physicians and people with MS choosing to switch from natalizumab to fingolimod should initiate treatment within 8–12 weeks after natalizumab discontinuation (for reasons other than pregnancy or pregnancy planning) to diminish the return of disease activity (Level B).

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

American College of Gastroenterology

According to the 2018 American College of Gastroenterology Practice Guidelines for the Management of Crohn's Disease in Adults (ACG Practice Guideline), patients with moderate-severe disease usually have a Crohn's Disease Activity Index (CDAI) of 220-450. They have failed to respond to treatment for mild-moderate disease, or have more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting (without obstructive findings), or significant anemia. They typically have moderate to severely active endoscopic mucosal disease.

The 2018 ACG Practice Guideline states that:

- Natalizumab is more effective than placebo and should be considered to be used for induction of symptomatic response and remission in patients with active Crohn's disease (strong recommendation, high level of evidence).
- Natalizumab should be used for maintenance of natalizumab-induced remission of Crohn's disease only if serum antibody to John Cunningham (JC) virus is negative. Testing for anti-JC virus antibody should be repeated every 6 months and treatment stopped if the result is positive. (strong recommendation, moderate level of evidence).
- Natalizumab should be considered for maintaining remission of natalizumab-induced remission of Crohn's disease patients only if John Cunningham (JC) virus is negative (conditional recommendation, moderate level of evidence).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Natalizumab is 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. Natalizumab increases the risk of PML. When initiating and continuing treatment with natalizumab, physicians should consider whether the expected benefit of natalizumab is sufficient to offset this risk.

Natalizumab is also 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. Natalizumab should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α.

Tysabri is available only through a risk minimization plan called Tysabri Outreach Unified Commitment to Health (the TOUCH® Prescribing Program) which registers prescribers, infusion centers, and pharmacies associated with infusion centers. Additionally, Tysabri can only be prescribed to patients who are enrolled in and meet all the requirements of the program. Additional details and requirements in regard to the program may be found at: https://www.touchprogram.com/TTP/.

Tyruko is available only through a risk minimization plan which registers prescribers, infusion centers, and pharmacies associated with infusion centers. Additionally, Tyruko can only be prescribed to patients who are enrolled in and meet all the requirements of the program. Additional details and requirements in regard to the program may be found at: https://www.tyruko-rems.com/#Main/!Main/Home.

Centers for Medicare and Medicaid Services (CMS)

Coverage guidelines for certain Part B drugs may be found in the Medicare Advantage Medical Policy titled Medications/Drugs (Outpatient/Part B). National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. These NCDs/LCDs/LCAs are available at https://www.cms.gov/medicare-coverage-database/new-search/search.aspx.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that certain criteria are met, including that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals.

*Preferred therapy criteria for Medicare Advantage members, refer to Medicare Part B Step Therapy Programs.

References

1. Tysabri [package insert]. Biogen Idec, Inc: Cambridge, MA; March 2025.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

2. Tramacere I, Del Giovane C, Salanti G, et al. Immunomodulators and immunosuppressants for relapsing-remitting multiple sclerosis: a network meta-analysis. Cochrane Database Syst Rev. 2015 Sep 18;(9):CD011381.
3. Goodin DS, Frohman EM, Garmany JP, et al. Disease modifying therapies in multiple sclerosis: Report of the Therapeutics and Technology Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology 2002;58;169.
4. 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; Apr 24;90.
5. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Practice Guidelines. Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018 Apr;113(4):481-517.
6. Crohn's Disease information page. National Digestive Diseases Information Clearinghouse (NDDIC) Web site. Available at https://www.niddk.nih.gov/health-information/digestive-diseases/crohns-disease. Accessed March 24, 2022.
7. O'Connor P, Goodman A, Kappos L et al. Long-term safety and effectiveness of natalizumab redosing and treatment in the STRATA MS Study. Neurology. 2014 Jul 1;83(1):78-86.
8. Butzkueven H, Kappos L, Pellegrini F, et al. Efficacy and safety of natalizumab in multiple sclerosis: interim observational programme results. J Neurol Neurosurg Psychiatry. 2014 Nov;85(11):1190-7.
9. Nelson SM, Nguyen TM, McDonald JW, MacDonald JK. Natalizumab for induction of remission in Crohn's disease. Cochrane Database Syst Rev. 2018 Aug 1;8:CD006097.
10. Targan SR, Feagan BG, Fedorak RN, et al. Natalizumab for the Treatment of Active Crohn's Disease: Results of the ENCORE Trial. Gastroenterology. 2007;132(5):1672-83.
11. Expert Opinion Paper of the National Clinical Advisory Board of the National Multiple Sclerosis Society. Treatment Recommendations for Physicians: Patient Access to Tysabri. 2008.
12. Yoshida EM. The Crohn's Disease Activity Index, its derivatives and the Inflammatory Bowel Disease Questionnaire: A review of instruments to assess Crohn's disease. Can J Gastroenterol. 1999:13(1):65-73.
13. U.S. Food and Drug Administration Drug Safety Communication: New risk factor for Progressive Multifocal Leukoencephalopathy (PML) associated with Tysabri (natalizumab). https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-new-risk-factor-progressive-multifocal-leukoencephalopathy-pml. Accessed March 24, 2022.
14. U.S. Food and Drug Administration News Release: FDA permits marketing of First Test for risk of rare brain infection in some people treated with tysabri. Indo Global Journal of Pharmaceutical Sciences. https://www.iglobaljournal.com/fda-permits-marketing-of-first-test-for-risk-of-rare-brain-infection-in-some-people-treated-with-tysabri/. Accessed March 24, 2022.
15. Tyruko [package insert]. Sandoz, Inc: Princeton, NJ; August 2023.

Policy History/Revision Information

Date	Summary of Changes
07/01/2026	**Coverage Rationale** • Removed language indicating coverage criteria for Tyruko contained in this policy will be applicable immediately upon product launch • Removed content/language pertaining to preferred products **Supporting Information** • Updated *FDA*, *CMS*, and *References* sections to reflect the most current information • Archived previous policy version 2026D0026S

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

mandates. UnitedHealthcare reserves the right to modify its policies and guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.