BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.60.013

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	May 3, 2013
Subject:	Tysabri	**Page:**	1 of 7

Last Review Date: March 7, 2025

Tysabri

Description

Tysabri (natalizumab), Tyruko (natalizumab-sztn)*

*This medication is included in this policy but is not available on the market as of yet

Background
Tysabri (natalizumab) and its biosimilar are used to prevent episodes of symptoms and slow the worsening of disability in patients with relapsing forms (course of disease where symptoms flare up from time to time) of multiple sclerosis (MS). Tysabri and its biosimilar are also used to treat and prevent episodes of symptoms in people who have Crohn's disease (a condition in which the body attacks the lining of the digestive tract, causing pain, diarrhea, weight loss, and fever) who have not been helped by other medications or who cannot take other medications. Tysabri and its biosimilar are in a class of medications called immunomodulators. It works by stopping certain cells of the immune system from reaching the brain and spinal cord and causing damage (1-2).

Regulatory Status
FDA-approved indication: Tysabri and its biosimilar are integrin receptor antagonists indicated for treatment of (1-2):

Multiple Sclerosis (MS) - As monotherapy for the treatment of patients with relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Tysabri and its biosimilar increase the risk of PML. When initiating or continuing treatment with Tysabri or its biosimilar, physicians should consider whether the expected benefit of Tysabri or its biosimilar is sufficient to offset this risk.

Crohn's Disease (CD) - 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.

Limitations of Use: (1-2)
In Crohn's disease, Tysabri and its biosimilar should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α.

Tysabri and its biosimilar carry a boxed warning regarding the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. Tysabri and its biosimilar are contraindicated in patients who have or have had progressive multifocal leukoencephalopathy (PML). Monitor patients and withhold Tysabri and its biosimilar at the first sign or symptom suggestive of PML. Duration of Tysabri or its biosimilar exposure, prior immunosuppressant use, and presence of anti-JC virus antibodies are associated with increased risk of PML in patients treated with Tysabri or its biosimilar. There is limited experience in patients who have received more than 4 years of Tysabri or its biosimilar treatment (1-2).

The immune system effects of Tysabri and its biosimilar may increase the risk for infections. Concurrent use of antineoplastic, immunosuppressant, or immunomodulating agents may further increase the risk of infections, including PML, and other opportunistic infections, over the risk observed with the use of Tysabri or its biosimilar alone. Patients should be monitored for development of infections due to increased risk with use of Tysabri and its biosimilar (1-2).

The safety and efficacy of Tysabri and its biosimilar in combination with antineoplastic, immunosuppressant, or immunomodulating agents have not been established. Patients receiving chronic immunosuppressant or immunomodulatory therapy or who have systemic medical conditions resulting in significantly compromised immune system function should not ordinarily be treated with Tysabri or its biosimilar. The risk of PML is also increased in patients who have been treated with an immunosuppressant prior to receiving Tysabri or its biosimilar (1-2).

For patients with Crohn's disease who start Tysabri or its biosimilar while on chronic corticosteroids, commence steroid withdrawal as soon as a therapeutic benefit has occurred. If the patient cannot discontinue systemic corticosteroids within six months, discontinue Tysabri or its biosimilar (1-2).

Clinically significant liver injury has occurred. Signs of liver injury, including markedly elevated serum hepatic enzymes and elevated total bilirubin, occurred as early as six days after the first dose; signs of liver injury have also been reported for the first time after multiple doses. Tysabri and its biosimilar should be discontinued in patients with jaundice or evidence of liver injury (1-2).

Because of the risk of PML, Tysabri is available only under a restricted distribution program, the TOUCH Prescribing Program. Tyruko is available only under the Tyruko REMS Program (1-2).

Live, attenuated vaccines are generally not recommended for a person with MS because their ability to cause disease has been weakened but not totally inactivated (3).

According to the algorithm defined by Pharmacotherapy: A Pathophysiologic Approach for the management of clinically definite multiple sclerosis, it may be reasonable for patients with severe disease to use a monoclonal antibody without having tried other MS therapies (4).

Safety and effectiveness of Tysabri and its biosimilar in pediatric patients with multiple sclerosis or Crohn's disease below the age of 18 years have not been established. Tysabri and its biosimilar are not indicated for use in pediatric patients (1-2).

Related policies

Acthar Gel, Ampyra, Aubagio, Briumvi, Gilenya, Kesimpta, Lemtrada, Mavenclad, Mayzent, MS Injectables, Ocrevus, Ponvory, Tecfidera, Zeposia

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Tysabri and its biosimilar may be considered **medically necessary** if the conditions indicated below are met.

Tysabri and its biosimilar may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Relapsing Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease
    a. Used as monotherapy
    b. **NOT** used in combination with another MS disease modifying agent

2. Crohn's Disease (CD)
    a. Moderately to severely active
    b. Inadequate treatment response, intolerance, or contraindication to **ALL** of the following:
        i. Conventional Crohn's disease therapies
        ii. TNF inhibitors
    c. **NOT** used in combination with immunosuppressants or TNF inhibitors

AND ALL of the following for **ALL** indications:

a. Patient does **NOT** have or have had progressive multifocal leukoencephalopathy (PML)
b. Patient will be monitored for any new sign or symptom that may be suggestive of PML
    i. Medication will be withheld at the 1st sign or symptom suggestive of PML
c. Patient does **NOT** have significantly compromised immune system function
d. **NOT** given concurrently with live vaccines
e. **Tysabri ONLY:** Patient must be enrolled in and meet all conditions of the TOUCH Prescribing Program
f. **Tyruko ONLY:** Patient must be enrolled in and meet all conditions of the Tyruko REMS Program

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Relapsing Multiple sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease
    a. Used as monotherapy
    b. **NOT** used in combination with another MS disease modifying agent

2. Crohn's Disease (CD)
    a. **NOT** used in combination with immunosuppressants or TNF inhibitors
    b. Patient has experienced therapeutic benefit by 12 weeks of induction therapy

AND ALL of the following for **ALL** indications:

a. Patient does not have progressive multifocal leukoencephalopathy (PML)
b. **NO** concurrent therapy with systemic corticosteroids
c. **NO** evidence of jaundice or liver injury
d. **NO** development of opportunistic infections
e. **NO** development of herpes infections
f. **NOT** given concurrently with live vaccines
g. **Tysabri ONLY:** Patient must be enrolled in and meet all conditions of the TOUCH Prescribing Program
h. **Tyruko ONLY:** Patient must be enrolled in and meet all conditions of the Tyruko REMS Program

Policy Guidelines

Pre – PA Allowance

None

Prior – Approval Limits

Duration 4 months

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary

Tysabri (natalizumab) and its biosimilar are used to prevent episodes of symptoms and slow the worsening of disability in patients with relapsing forms of multiple sclerosis. Tysabri and its biosimilar are also used to treat and prevent episodes of symptoms in people who have Crohn's disease who have not been helped by other medications or who cannot take other medications. In CD, Tysabri and its biosimilar should not be used in combination with immunosuppressants or inhibitors of TNF-α. Tysabri and its biosimilar carry a boxed warning regarding the risk of progressive multifocal leukoencephalopathy (PML). The immune system effects of Tysabri and its biosimilar may increase the risk for infections. The safety and efficacy of Tysabri and its biosimilar in combination with antineoplastic, immunosuppressant, or immunomodulating agents have not been established. Tysabri and its biosimilar should be discontinued in patients with jaundice or evidence of liver injury. Because of the risk of PML, Tysabri is available only under a special restricted distribution program, the TOUCH prescribing program. Tyruko is available only under the Tyruko REMS program. Tysabri and its biosimilar are not indicated for use in pediatric patients (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Tysabri and its biosimilar while maintaining optimal therapeutic outcomes.

References

1. Tysabri [package insert]. Cambridge, MA: Biogen Inc.; October 2023.
2. Tyruko [package insert]. Princeton, NJ: Sandoz Inc.; August 2023.
3. Cahill JF, Izzo A, Garg N. Immunization in patients with multiple sclerosis. Neurological Bulletin. 2010;2(1):17-21.
4. Bainbridge, Jacquelyn L., et al. "Multiple Sclerosis." Pharmacotherapy: A Pathophysiologic Approach, 11e, 2020. Available at: https://accesspharmacy.mhmedical.com/content.aspx?bookid=2577&sectionid=231921409.

Policy History

Date	Action
May 2013	Addition to PA
September 2014	Annual editorial review and reference update Removal of evidence of inflammation
December 2014	Annual editorial review and reference update
March 2015	Annual editorial review and reference update
September 2016	Annual editorial review and reference update Policy number changed from 5.08.27 to 5.60.13

December 2016	Addition of age limits to renewal criteria Change in duration of prior approval limits for initiation from 6 months to 4 months Addition of not given concurrently with live vaccines to MS indication
March 2017	Annual review
June 2017	Annual review
November 2018	Annual editorial review and reference update. Addition of no development of herpes infections to renewal requirements
September 2019	Annual review. Revised relapsing MS indication to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease
March 2020	Annual review
September 2020	Annual review and reference update
December 2020	Annual review
June 2021	Annual review
December 2022	Annual review and reference update. Changed policy number to 5.60.013. Per SME, added caveat that t/f of an MS therapy does not apply if the patient has advanced, progressive, or severe disease
June 2023	Annual editorial review. Added requirement for MS of no dual therapy with another MS disease modifying agent
December 2023	Annual editorial review and reference update. Addition of biosimilar Tyruko
September 2024	Per FEP, removed requirement to t/f 2 MS treatments for relapsing MS
December 2024	Annual review and reference update
March 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.