



**BlueCross  
BlueShield**

Federal Employee Program.

Federal Employee Program®  
1310 G Street, N.W.  
Washington, D.C. 20005  
202.942.1000  
Fax 202.942.1125

# 5.60.013

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2024
<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	May 3, 2013
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**Last Review Date:** December 8, 2023

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## 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 Tyruko (natalizumab-sztn) 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/Tyruko 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/Tyruko 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 Tyruko 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 Tyruko increase the risk of PML. When initiating or continuing treatment with Tysabri/Tyruko, physicians should consider whether the expected benefit of Tysabri/Tyruko is sufficient to offset this risk.

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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- $\alpha$ .

Limitations of Use: (1-2)

In Crohn's disease, Tysabri and Tyruko should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF- $\alpha$ .

Tysabri and Tyruko 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/Tyruko is contraindicated in patients who have or have had progressive multifocal leukoencephalopathy (PML). Monitor patients and withhold Tysabri/Tyruko at the first sign or symptom suggestive of PML. Duration of Tysabri/Tyruko exposure, prior immunosuppressant use, and presence of anti-JC virus antibodies are associated with increased risk of PML in patients treated with Tysabri/Tyruko. There is limited experience in patients who have received more than 4 years of Tysabri/Tyruko treatment (1-2).

The immune system effects of Tysabri and Tyruko 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/Tyruko alone. Patients should be monitored for development of infections due to increased risk with use of Tysabri/Tyruko (1-2).

The safety and efficacy of Tysabri and Tyruko 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/Tyruko. The risk of PML is also increased in patients who have been treated with an immunosuppressant prior to receiving Tysabri/Tyruko (1-2).

For patients with Crohn's disease who start Tysabri and Tyruko 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/Tyruko (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

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dose; signs of liver injury have also been reported for the first time after multiple doses. Tysabri and Tyruko 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 Tyruko in pediatric patients with multiple sclerosis or Crohn's disease below the age of 18 years have not been established. Tysabri/Tyruko is 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 Tyruko may be considered **medically necessary** if the conditions indicated below are met.

Tysabri and Tyruko 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

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- a. Used as monotherapy
- b. Inadequate treatment response, intolerance, or contraindication to another MS therapy
  - i. Does not apply if the patient has advanced, progressive, or severe disease
- c. **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 1<sup>st</sup> 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:

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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

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Tysabri (natalizumab) and Tyruko (natalizumab-sztn) are used to prevent episodes of symptoms and slow the worsening of disability in patients with relapsing forms of multiple sclerosis. Tysabri/Tyruko is 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/Tyruko should not be used in combination with immunosuppressants or inhibitors of TNF- $\alpha$ . Tysabri/Tyruko carry a boxed warning regarding the risk of progressive multifocal leukoencephalopathy (PML). The immune system effects of Tysabri/Tyruko may increase the risk for infections. The safety and efficacy of Tysabri/Tyruko in combination with antineoplastic, immunosuppressant, or immunomodulating agents have not been established. Tysabri/Tyruko 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/Tyruko is 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 Tyruko while maintaining optimal therapeutic outcomes.

**References**

1. Tysabri [package insert]. Cambridge, MA: Biogen Inc.; April 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

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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

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.**