EVH Clinical Guideline 5035.CC for Natalizumab Products

Guideline Number:	Applicable Codes	
EVH_CG_5035.CC		
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Original Date:	**Last Revised Date:**	**Implementation Date:**
March 2022	June 2025	October 2025

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STATEMENT

General Information

- *It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Medical Policy Committee.*

- *If the established criteria are not met, the request is referred to a Medical Director for review, if required for the plan and level of request.*

Purpose

The purpose of this guideline to define the prior authorization process for the following natalizumab products: Tysabri® (natalizumab) and Tyruko® (natalizumab-sztn).

Scope

This guideline applies to all practitioners who are involved in providing the requested drug. This guideline is specific to the Health Plan's medical benefit.

INITIAL REVIEW CRITERIA

The request must meet all of the criteria listed below.

Crohn's Disease

- Must be prescribed by a gastroenterologist who is registered with the TOUCH Prescribing program
- Must be age 18 years or older
- Must have a diagnosis of moderately to severely active Crohn's disease or fistulizing Crohn's disease, as described in the 2018 ACG guidelines (see **Table 1**)
- Must have an adequate trial (of at least 3 months) and failure of at least one (1) of the following with an inadequate response, or significant side effects/toxicities, or have a contraindication to these therapies:
    - An adalimumab product
    - Cimzia
- Must have chart note documentation or an attestation from the provider of all the following:
    - Must not currently have or have a history of progressive multifocal leukoencephalopathy (PML)

- Must not be receiving 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

- Must have documentation of testing for anti-JCV antibodies
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Multiple Sclerosis

- Must be prescribed by a neurologist who is registered with the TOUCH Prescribing program
- Must have a diagnosis of a relapsing form of MS
  - Relapsing forms of MS include clinically isolated syndrome (CIS), relapsing-remitting disease, and active secondary progressive disease
- Must be age 18 years or older
- Must have previously had an inadequate response or intolerance to at least ONE of the following preferred multiple sclerosis therapies: Betaseron (interferon beta-1b), Copaxone (glatiramer acetate), Gilenya (fingolimod), Rebif (interferon beta-1a), or Tecfidera (dimethyl fumarate)
  - Only Gilenya (fingolimod) is required for members with "highly active" MS or considered to have prognostic factors of poorer clinical course
- Must have chart note documentation or an attestation from the provider of all the following:
  - 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
- Must have documentation of testing for anti-JCV antibodies
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

REAUTHORIZATION CRITERIA

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. The request must meet all of the criteria listed under the diagnosis-specific sections below.

Crohn's Disease

- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling
- Must have recent chart note documentation showing achievement or maintenance of a positive clinical response as evidenced by low disease activity OR improvement in at least ONE of the following from baseline:
  - Abdominal pain or tenderness
  - Diarrhea
  - Body weight
  - Abdominal mass
  - Hematocrit
  - Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
  - Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)
- Must have documentation or an attestation from the provider that there is no evidence of progressive multifocal leukoencephalopathy (PML)

Multiple Sclerosis

- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling
- Must have recent chart documentation from the provider that the member's condition has stabilized or improved based upon the prescriber's assessment while on therapy
- Must have documentation or an attestation from the provider that there is no evidence of progressive multifocal leukoencephalopathy (PML)

APPROVAL DURATIONS

Initial Authorization	Up to 1 year
Reauthorization	Same as initial

APPENDICES

Table 1 – 2018 ACG Clinical Guidelines Classification of Moderate-to-Severe Disease

Moderate-to-Severe Disease	Severe-Fulminant Disease
• CDAI 220-450 • Have failed treatment for mild to moderate disease • Prominent symptoms such as fever, weight loss, abdominal pain and tenderness, intermittent nausea or vomiting, or anemia • Moderate to severely active endoscopic mucosal disease	• CDAI >450 • Persistent symptoms despite glucocorticoids or biologic agents • Individuals presenting with high fever, persistent vomiting, intestinal obstruction, peritoneal signs, cachexia, or evidence of an abscess

CODING AND STANDARDS

Codes

Code	Brand	Description
J2323	Tysabri	Injection, Natalizumab, 1mg
Q5134	Tyruko	Injection, Natalizumab-sztn (Tyruko), biosimilar, 1mg

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☐	Commercial
☐	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

BACKGROUND

Tysabri® (natalizumab) 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).

POLICY HISTORY

Date	Summary
June 2025	• Added Tyruko • Updated initial and reauthorization criteria for both diagnoses (e.g., included dosing criterion, updated diagnostic criteria for Crohn's, updated prerequisite requirements for both diagnoses)
February 2023	• Updated approval durations to 1 year
March 2022	• New Guideline

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Administrative Services Medical Policy Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

Evolent Clinical Guidelines are comprehensive and inclusive of various procedural applications for each service type. Our guidelines may be used to supplement Medicare criteria when such criteria is not fully established. When Medicare criteria is determined to not be fully established, we only reference the relevant portion of the *corresponding Evolent Clinical Guideline that is applicable to the specific service or item requested in order to determine medical necessity.*

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