Multiple Sclerosis Agents: natalizumab (Tysabri)

WA.PHAR.148 Effective Date: 7/1/2025

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current publication of the Coordinated Care of Washington, Inc. Preferred Drug List (PDL), please visit: *https://www.coordinatedcarehealth.com/content/dam/centene/centene-pharmacy/pdl/FORMULARY-CoordinatedCare_Washington.pdf*

Medical necessity:

Drug	Medical Necessity
natalizumab (Tysabri)	**Natalizumab (Tysabri)** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Crohn's Disease natalizumab (Tysabri)	Natalizumab (Tysabri) may be approved when all the following documented 1. Patient is 18 years of age or older; **AND** 2. Prescribed by, or in consultation with a gastroenterologist; **AND** 3. Not used in combination with another Cytokine and CAM medication; **AND** 4. Diagnosis of moderate to severe Crohn's disease (CD); **AND** a. Treatment with conventional therapy has been ineffective, unless all are contraindicated, or not tolerated. Conventional therapy is defined as: i. Oral corticosteroids (e.g., prednisone, methylprednisolone) used short-term to induce remission or alleviate signs/symptoms of disease flare; **AND** ii. At least one immunomodulatory agent (e.g., methotrexate, azathioprine, 6-mercaptopurine) [minimum trial of 12 weeks]; **OR** b. Documentation of high-risk disease (e.g., symptoms despite conventional therapy, obstruction, abscess, stricture, phlegmon, fistulas, resection, extensive bowel involvement, early age of onset, growth retardation, Crohn's Disease

	Activity Index (CDAI) > 450, Harvey-Bradshaw index > 7); **AND** 5. Treatment with two preferred Cytokine and CAM Apple Health Preferred Drug List (PDL) medications has each been ineffective, unless all are contraindicated or not tolerated [minimum trial of 12 weeks]. If ALL criteria are met, the request will be authorized for **6 months.** **Criteria (Reauthorization)** Natalizumab (Tysabri) may be approved when all the following documented criteria are met: 1. Not used in combination with another Cytokine and CAM medication; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., improvement in endoscopic activity, taper or discontinuation of corticosteroids, reduction in number of liquid stools, decrease in presence and severity of abdominal pain, decrease in CDAI, decrease in Harvey-Bradshaw index). If ALL criteria are met, the request will be authorized for **12 months.**
Multiple Sclerosis natalizumab (Tysabri)	Natalizumab (Tysabri) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Prescribed by, or in consultation with a neurologist; **AND** 3. Not used in combination with other disease modifying therapies (DMTs) for multiple sclerosis; **AND** 4. Diagnosis of one of the following: a. Relapsing remitting disease (RRMS); **OR** b. Active secondary progressive disease (SPMS); **OR** c. Clinically isolated syndrome; **AND** 5. Diagnosis is confirmed and documented by a laboratory report (e.g. MRI); **AND** 6. Documentation of baseline number of relapses per year or expanded disability status scale (EDSS score); **AND** 7. Treatment with two preferred Multiple Sclerosis Apple Health Preferred Drug List (PDL) medications has been ineffective, unless all are contraindicated, or not tolerated. If ALL criteria are met, the request will be authorized for **12 months.** **Criteria (Reauthorization)** Natalizumab (Tysabri) may be approved when all the following documented criteria are met: 1. Not used in combination with other disease modifying therapies (DMTs) for multiple sclerosis**; AND**

	2. Documentation is submitted demonstrating disease stability or a positive clinical response (i.e., decrease in number of relapses per year, improvement in EDSS score). If ALL criteria are met, the request will be authorized for **12 months.**

Dosage and quantity limits:

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
Tysabri	Crohn's Disease	300mg every 4 weeks	• 300mg/15mL vial: 300 BU per 28 days
	Multiple Sclerosis	300mg every 4 weeks	• 300mg/15mL vial: 300 BU per 28 days

Coding:

HCPCS Code	Description
J2323	Injection, natalizumab, 1 mg; 1 billable unit = 1mg (*Tysabri Only*)

Background:

Crohn's Disease

Therapeutic recommendations for patients with Crohn's disease (CD) are established based upon disease location, disease severity, disease associated complications, and future disease prognosis. The goals of therapy are to induce remission, prevent relapse, and prevent occurrence of disease complications, such as stricture and fistula. According to the 2018 American College of Gastroenterology (ACG) guidelines, for patients with moderate to severe disease and those with moderate to high-risk disease treatment with oral corticosteroids used short term to induce remission is recommended (strong recommendation, moderate level of evidence). However, it is noted that one in five patients will become steroid refractory which is thought to be the result of unreliable efficacy in healing of the mucosa associated with steroids (weak recommendation, low level of evidence). Corticosteroids are also implicated in the development of perforating complications (abscess and fistula) and are relatively contraindicated in those patients. The 2021 American Gastroenterological Association (AGA) clinical guidelines make similar recommendations and suggest the use of corticosteroids in adult outpatients with moderate to severe CD over no treatment for induction of remission (conditional recommendation, moderate level of evidence). In patients with moderate to severe CD who remain symptomatic despite current or prior corticosteroid therapy, 2018 ACG guidelines recommend immunomodulators such as azathioprine, 6-mercaptopurine (strong recommendation, moderate level of evidence), and methotrexate (conditional recommendation, low level of evidence) to be effective for maintenance of remission. Due to slow time to clinical response that may not be evident for as long as 12 weeks, these agents are not recommended for short-term induction. The 2021 AGA guidelines make similar suggestions and recommend use of thiopurines over no treatment for the maintenance of remission (conditional recommendation, low level of evidence). The timing of introduction of biologic agents is a matter of debate and more studies are needed to assess stepwise approach versus earlier administration of biologic agents in patients with moderate to severe disease. The 2019 British Society of Gastroenterology guidelines suggest that systemic corticosteroids are still an effective initial therapy for uncomplicated luminal moderate to severe disease, regardless of disease location; however, every effort should be made to limit exposure (strong recommendation, high-quality evidence). In patients with an aggressive disease course, or high risk, poor prognostic factors, early introduction of biologics may be considered (weak recommendation, moderate-quality evidence). High risk features include extensive disease, complex (stricturing or penetrating disease), perianal fistulizing disease, age under 40 years at diagnosis, and the need for steroids to control index flare; however, the predictive power of these features is limited.

Multiple Sclerosis

The American Academy of Neurology (AAN) 2019 practice guidelines note disease-modifying therapy (DMT) as the current standard of treatment for MS. Clinical evidence suggests DMT therapy is reasonably effective in managing MS, as data shows that on average, annualized relapse rates for MS patients in the United States drop from 0.46-1.8

to 0.18-0.49 relapses per year after management with DMT. Guidelines and consensus statements by the MS Coalition recommend clinicians should offer DMTs to people with relapsing forms of MS with recent clinical relapses or MRI activity. While both bodies advocate for a wide range of therapy options for patients sequential treatment recommendations are not made. Per the MS Coalition consensus statement clinicians should consider prescribing a high efficacy medication such as alemtuzumab, cladribine, fingolimod, ocrelizumab or natalizumab for newly diagnosed individuals with highly active MS.

Management of Immune Checkpoint Inhibitor-Related Diarrhea/Colitis
The primary facets of immune-related adverse event (irAE) management include recognition and grading of toxicity, immunosuppression, and individualized modification to ICI administration. Early recognition of symptoms and prompt intervention are key goals for the management of immunotherapy-related toxicity. Significant irAEs often necessitate holding immunotherapy, with permanent discontinuation of the class of agent associated with the toxicity in the setting of certain severe irAEs. Per NCCN guidelines for the Management of Immunotherapy Related Toxicities corticosteroids are the mainstay treatment for ICI-related toxicity; however, severe or steroid-refractory irAEs may require administration of additional immunosuppressive agents. Recommendation for use of specific immune-modulating agents to manage irAEs are typically extrapolated from evidence for treating autoimmune conditions of the relevant organ system. Case reports have described the use of vedolizumab for treating ICI-induced enterocolitis. Vedolizumab may provide more specific immune suppression for the inflamed GI mucosa, hence theoretically sparing systemic immune suppression and anti-tumor immune responses. Case series and reports have also documented successful treatment of ICI-mediated, steroid-dependent, or steroid-refractory enterocolitis with vedolizumab.

References:

1. Tysabri [package Insert]. Cambridge, MA; Biogen, Inc.; April 2023. Accessed February 2024.
2. National Institute for Health and Care Excellence. NICE 2019. Crohn's Disease: Management. Published 03 May 2019. Clinical Guideline [NG129]. https://www.nice.org.uk/guidance/ng129/resources/crohns-disease-management-pdf-66141667282885
3. Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021;160(7):2496-2508. doi:10.1053/j.gastro.2021.04.022
4. American Academy of Neurology. Practice Guideline: Disease-modifying Therapies for Adults with Multiple Sclerosis. 2018; https://www.aan.com/Guidelines/home/GetGuidelineContent/900.
5. Costello K and Kalb R. The Use of Disease-Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence. Consensus Paper by the Multiple Sclerosis Coalition. 2019.

History:

Approved Date	Effective Date	Version	Action and Summary of Changes
08.14.2024	07.01.2025	62.40.50.AA-1	- Split Tysabri from CAC policy
08.14.2024	04.01.2025	66.27.00.AD-5	- Added language for preferred adalimumab biosimilars - Formatting updates
08.14.2024	03.01.2025	66.27.00.AD-4	Approved by DUR Board - Split 66.27.00 policy into different policies -Added new drug indications when applicable -Update language in medical necessity section
Previous policy changes (relevant from Cytokine & CAM Antagonists Policy)			
Date			**Action and Summary of Changes**

10.21.2021	Removed Hyrimoz from the policy and updated the initial dosing for infliximab.
11.30.2020	Removed Preferred/Non-Preferred listing and added link to AHPDL publication
11.12.2020	Added language in clinical policy section for cases which do not meet policy criteria
09.01.2020	Updated wording in clinical criteria for products with only one preferred option.
08.19.2020	Approved by DUR Board
08.20.2020	Update to dosing and limits section for all products and indications
08.12.2020	Updated policy clinical criteria and dosing & quantity limits to include nonradiographic axial spondyloarthritis
06.01.2020	Added new agents to class; updated age limit for Uveitis indication; updated dosing and quantity limits; updated HCPCS coding
07.31.2019	Updated criteria that trial of preferred biologics only applies to non-preferred biologics
06.07.2019	Updates to TB skin test requirements for apremalist; updates to initial authorization clinical criteria
11.02.2018	Addition of Hyrimoz (adalimumab-adaz)
09.07.2018	Addition of new medication
08.16.2017	New Policy

Appendix:

<table>
<tr><th colspan="2">MS with a relapsing-remitting course (RRMS)</th></tr>
<tr><td colspan="2">• Based upon two separate areas of damage (dissemination in space) in the CNS that have occurred at different points in time (dissemination in time). Unless contraindicated, MRI should be obtained.</td></tr>
<tr><td>Dissemination in time (Development/appearance of new CNS lesions over time)</td><td>Dissemination in space
(Development of lesions in distinct anatomical locations within the CNS)</td></tr>
<tr><td>• ≥ 2 clinical attacks; OR
• 1 clinical attack AND one of the following:
○ MRI indicating simultaneous presence of gadolinium-enhancing and non-enhancing lesions at any time or by a new T2-hyperintense or gadolinium-enhancing lesion on follow-up MRI compared to baseline scan
○ CSF-specific oligoclonal bands</td><td>• ≥ 2 lesions; OR
• 1 lesion AND one of the following:
○ Clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location
○ MRI indicating ≥ 1 T2-hyperintense lesions characteristic of MS in ≥ 2 of 4 areas of the CNS (periventricular, cortical or juxtacortical, infratentorial, or spinal cord)</td></tr>
<tr><th colspan="2">Secondary progressive MS course</th></tr>
<tr><td colspan="2">• MS course characterized by steadily increasing objectively documented neurological disability independent of relapses. Fluctuations, periods of stability, and superimposed relapses might occur. Secondary progressive multiple sclerosis, is further distinguished as a progressive course following an initial relapsing-remitting course.</td></tr>
</table>

- Diagnosed retrospectively based on previous year's history.

Secondary Progressive MS (SPMS)

Active secondary progressive MS (SPMS) is defined as the following:

- Expanded Disability Status Scale (EDSS) score ≥ 3.0; **AND**
- Disease is progressive ≥ 3 months following an initial relapsing-remitting course (i.e., EDSS score increase by 1.0 in patients with EDSS ≤5.5 or increase by 0.5 in patients with EDSS ≥6); **AND**
  - ≥ 1 relapse within the previous 2 years; **OR**
  - Patient has gadolinium-enhancing activity OR new or unequivocally enlarging T2 contrast-enhancing lesions as evidenced by MRI

Clinically Isolated Syndrome (CIS)

Definitive diagnosis of Clinically Isolated Syndrome (CIS) is based upon ALL of the following

- A monophasic clinical episode with patient-reported symptoms and objective findings reflecting a focal or multifocal inflammatory demyelinating event in the CNS
- Neurologic symptom duration of at least 24 hours, with or without recovery
- Absence of fever or infection
- Patient is not known to have multiple sclerosis