PART B DRUG MEDICAL/PHARMACY	ASPIRE HEALTH	Effective Date January 1, 2024	
	TYSABRI (NATALIZUMAB)	Policy # Tysabri (natalizumab)	
		Review Date 11/29/2023	**Applicable to:** ☑ Medicare Advantage ☐ Commercial ☐ Elevance Health HMO ☐ Blue Shield Trio
	Approver's Name & Title QI & UM Drug Subcommittee		

Aspire Health Plan (AHP) applies medical drug clinical criteria as a reference for medical policy information only. Federal and state laws or requirements, contract language, and Plan benefit may take precedence over the application of these clinical criteria. Please consult the applicable certificate or contract for benefit details. This policy is subject to revision at the discretion of the Plan and is therefore subject to change. Refer to the disclaimer section below for more information.

POLICY

This policy addresses the coverage of Tysabri (natalizumab) in the treatment of Crohn's disease and relapsing forms of multiple sclerosis.

APPLICABLE HCPCS

J2323: Injection, natalizumab, 1 mg; 1 billable unit = 1mg

Available Dosage Form: Tysabri 300 mg/15 mL single-use vial

CLINICAL CRITERIA

A. INITIAL CRITERIA

Tysabri (natalizumab) may be authorized when **ALL** of the following criteria have been met with documentation (i.e., office chart notes, treatment response to previous therapy or drug regimens, lab results, treatment plan, other relevant clinical information).

1. Documented diagnosis of **ONE** of the following:
    a. Moderately to severely active Crohn disease; **OR**
    b. Relapsing forms of multiple sclerosis:
        i. Active Secondary Progressive Multiple Sclerosis (SPMS) (e.g., SPMS with a documented relapse); or
        ii. Clinically Isolated Syndrome; or
        iii. Relapsing-Remitting Multiple Sclerosis.

AND

2. Prescribed by, or in consultation with, a specialist in the area of member's diagnosis (e.g., gastroenterologist for the diagnosis of Crohn's Disease or neurologist for the diagnosis of MS); **AND**

3. Member meets **ONE** (a or b) of the following criteria according to documented diagnosis:

    a. For Crohn's Disease

        i. Documentation of failure, contraindication or intolerance to **ONE** anti-tumor necrosis factor (anti-TNF) biologic (e.g., infliximab, adalimumab, certolizumab pegol [Cimzia®]); **AND**

        ii. Member will NOT be using natalizumab (Tysabri) in combination with an immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) for the requested indication.

    b. Relapsing Forms of Multiple Sclerosis

        i. Clinical relapse occurring during previous 12 months; **AND**

        ii. Member will NOT be using natalizumab (Tysabri) in combination with another disease-modifying therapies for MS: daclizumab (Zinbryta®), glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), fingolimod (Gilenya™), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), and ocreliuzmab (Ocrevus™).

AND

4. Member has been evaluated for anti-JC virus antibodies before initiation of natalizumab; **AND**

5. Member does NOT have the following conditions:

    a. Current or past history of progressive multifocal leukoencephalopathy (PML); **and**

    b. Systemic medical condition causing compromised immune system function (e.g., HIV disease, hematologic malignancy).

AND

6. Prescriber is certified with, and patient is enrolled in, Tysabri Outreach Unified Commitment to Health (TOUCH) program.

B. REAUTHORIZATION / CONTINUATION OF THERAPY CRITERIA

Tysabri (natalizumab) may be authorized for continuation of therapy when the initial criteria have been met **AND** documentation of the following:

1. Absence of intolerance or adverse events from the previous course of treatment [e.g., hypersensitivity reactions/antibody formation, hepatotoxicity, signs or symptoms of PML, herpes infections (including herpes encephalitis and meningitis and acute retinal necrosis), immunosuppression, infections (including pneumonias, pneumocystis carinii pneumonia, pulmonary mycobacterium avium intracellulare, bronchopulmonary aspergillosis, herpes, urinary tract infections, gastroenteritis, vaginal infections, tooth infections, tonsillitis, etc.), thrombocytopenia, etc.]

2. Not prescribed for, or administered concurrently with, other disease-modifying therapies for MS; **AND**

3. Positive response to therapy indicated by **ONE** of the following as applicable to member's diagnosis:

    a. **Multiple Sclerosis.** Documentation of stabilization or improvement in disease activity, signs and symptoms, or functional capacity as compared to baseline (or prior to treatment with Tysabri [natalizumab]):

        i. A decrease in frequency, severity, sequelae relapses from baseline; or

        ii. Beneficial effect on MRI measures of disease severity; or

        iii. Improvement in patients reported MS related symptoms.

    b. **Crohn's Disease.** Documentation of remission of disease or improved disease activity [e.g., stability or improvement include laboratory assessment (CRP, hemoglobin, ESR, WBC, albumin), or symptom assessment (e.g., bleeding, stooling pattern, abdominal pain, extraintestinal complaints, fatigue), or endoscopy results:

        i. Initial authorization: May be authorized for 12 weeks for members with a documented clinical response and remission of disease.

        ii. For second renewal only: Member has been tapered off oral corticosteroids within 6 months of starting Tysabri; AND Documented clinical response and remission of disease as indicated in the 'Reauthorization' criteria above.

            NOTE: If the member cannot be tapered off oral corticosteroids within 6 months of starting treatment, discontinue natalizumab.

        iii. All subsequent renewals: Member does not require additional steroid use that exceeds 3 months in a calendar year to control their Crohn's disease; AND documented clinical response and remission of disease as indicated in the 'Reauthorization' criteria above.

STEP THERAPY

Step therapy criteria do not apply for members who are currently being treated with the requested medications. Step therapy is only applied for members that are new to therapy (have not received the requested drug in the last 365 days.

PREFERRED PRODUCT: No step therapy required.

QUANTITY AND AUTHORIZATION PERIOD

1. Recommended Dose (all Indications): Administer 300 mg intravenously over one hour every 4 weeks.

2. Maximum Dose / Quantity:

    a. 300 mg for each infusion; 1 vial (Tysabri 300 mg/15 mL vial): per 28 days.

    b. Max Units (per dose and over time): 300 billable units every 28 days.

3. Authorization Period

   a. Crohn's Disease

      i. Initial authorization: May be authorized for 12 weeks for members with a documented clinical response and remission of disease as indicated in the 'Reauthorization' criteria above.

      ii. For second reauthorizations: Member has been tapered off oral corticosteroids within 6 months of starting Tysabri; **AND** Documented clinical response and remission of disease as indicated in the 'Reauthorization' criteria above. **NOTE:** If the member cannot be tapered off oral corticosteroids within 6 months of starting treatment, discontinue natalizumab.

      iii. All subsequent renewals: Member does not require additional steroid use that exceeds 3 months in a calendar year to control their Crohn's disease; **AND** documented clinical response and remission of disease as indicated in the 'Reauthorization' criteria above.

   b. Multiple Sclerosis: Initial and continuation of authorization: May be authorized for up to for 6 months.

DRUG INFORMATION

PHARMACOLOGIC CATEGORY: Monoclonal Antibody, Selective Adhesion-Molecule Inhibitor

ROUTE OF ADMINISTRATION: Intravenous Infusion

FDA-APPROVED USES:

1. Crohn disease**:** Inducing and maintaining clinical response and remission in adults with moderately to severely active Crohn disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional Crohn disease therapies and inhibitors of tumor necrosis factor-alpha (TNF-alpha).
2. Multiple sclerosis, relapsing: As monotherapy for the treatment of patients with relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease. Natalizumab increases the risk of progressive multifocal leukoencephalopathy. When initiating and continuing treatment with natalizumab, consider whether the expected benefit of natalizumab is sufficient to offset this risk.

COMPENDIAL APPROVED OFF-LABELED USES: None
Off-Label / Investigational Uses: Requests for off-label uses with a paucity of clinical evidence, or uses that are not generally accepted by the medical community (such as professional guidelines or consensus), CMS-recognized compendia, or peer-reviewed literature is considered investigational and will not be authorized due to insufficient evidence of overall therapeutic value of safety and efficacy.

BOXED WARNING: Progressive multifocal leukoencephalopathy (PML)
Tysabri (natalizumab) increases the risk of PML. Risk factors for the development of PML include the presence of anti-JC virus antibodies, duration of therapy, and prior use of immunosuppressants. These factors should be considered in the context of expected benefit when initiating and continuing treatment. Monitor for any new sign or symptom that may be suggestive of PML. Dosing should be withheld immediately at the first sign or symptom suggestive of PML. For diagnosis, an evaluation that includes a gadolinium-enhanced MRI scan of the brain and, when indicated, cerebrospinal fluid analysis for JC viral DNA are recommended.

CONTRAINDICATIONS:
Hypersensitivity to natalizumab or any component of the formulation; current or history of PML.

OTHER CONSIDERATIONS

- Risk Evaluation and Mitigation Strategy (REMS) PROGRAM: Tysabri (natalizumab) 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. Only prescribers registered in the TOUCH Prescribing Program may prescribe natalizumab. Additionally, Tysabri can only be prescribed to patients who are enrolled in and meet all the requirements of the program. For prescribers and patients, the TOUCH® Prescribing Program has two components: MS TOUCH® (for patients with multiple sclerosis) and CD TOUCH® (for patients with Crohn's disease). Patients must be enrolled in the TOUCH® Prescribing Program, read the Medication Guide, understand the risks associated with Tysabri, and complete and sign the Patient-Prescriber Enrollment Form. Pharmacies and infusion centers must be specially certified to dispense or infuse Tysabri.
- Limitations: Non-Relapsing Forms of Multiple Sclerosis. The safety and efficacy of Tysabri have not been established in patients with primary progressive multiple sclerosis

CLINICAL SUMMARY / APPENDIX

The American Academy of Neurology (AAN) published practice guidelines in 2018 regarding disease-modifying therapies for adults with MS. The guidelines recommend initiating disease-modifying therapy in patients with relapsing forms of MS who have recently experienced clinical relapses or MRI activity. The guidelines also recommend DMT for individuals who have experienced a single clinical demyelinating event and two or more brain lesions consistent with MS, if the individual wishes to initiate therapy after a discussion of risks and benefits. The guidelines do not specify a preferred DMT. However, some DMTs were recommended for certain MS subpopulations, including a recommendation for Tysabri for highly active disease.

REFERENCES

Government Agency

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database: National coverage determination (NCD) (search: Tysabri, natalizumab). Available from CMS. No NCD identified (LCD available but not applicable to MAC)**.**
2. CMS IOM, Publication 100-02, Medicare Benefit Policy Manual, Chapter 15, Section 50.4.5
3. CMS Transmittal 96, Change Request (CR) 6191 .

Prescribing Information

Tysabri (natalizumab) [prescribing information]. Cambridge, MA: Biogen Inc; April 2023.

Peer Reviewed Literature, Guidelines

1. Milliman Care Guidelines (MCG). Ambulatory Care 27th Edition ACG: A-0469 (AC). 2023.
2. Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG clinical guideline: management of Crohn's disease in adults. American Journal of Gastroenterology 2018;113(4):481-517. DOI: 10.1038/ajg.2018.27.
3. Olek MJ, Howard J. Clinical presentation, course, and prognosis of multiple sclerosis in adults. González-Scarano, F. (ed). UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed September 2023.
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; 90: 777-788. Available from: AAN. Accessed September 2023.

IMPORTANT REMINDER

This Medicare Part B Step Therapy Medical Necessity Guideline is provided for informational purposes only and neither constitutes nor replaces professional medical advice. Physicians, hospitals, and other providers are expected to administer or use drugs/biologicals in the most effective and clinically appropriate manner. Treating physicians and other health care providers are solely responsible for all medical care decisions. In accordance with the member's Evidence of Coverage (EOC), every benefit plan has its own coverage provisions, limitations, and exclusions. In the event of a conflict between this policy and the member's EOC, the member's EOC provisions will take precedence.

Aspire Health Plan (AHP) adheres to Medicare guidelines, including National Coverage Determination (NCD), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and other relevant Medicare manuals established by CMS. Compliance with these guidelines is required when applicable. Refer to the CMS website at http://www.cms.hhs.gov. For the most up-to-date Medicare policies and coverage, please search the Medicare Coverage Database. All LCDS are the same for each state within a Jurisdiction. Medicare Part B Administrative Contractor (MAC) for CA [Jurisdiction E (1)]: Active LCDs - JE Part B – Noridian (noridianmedicare.com). In the event of a discrepancy between this policy and the Medicare NCD or LCD, the Medicare NCD/LCD will govern.

This policy is utilized by AHP to determine coverage in the absence of applicable CMS Medicare guidelines. Please refer to the links provided in the References section below to access the Medicare source materials that were used for developing this resource document. This document does not serve as a substitute for the official Medicare source materials that provide detailed information on Medicare coverage requirements. In the event of a conflict between this document and Medicare source materials, the Medicare source materials will take precedence.

The inclusion of a code in this policy does not imply that the health service it describes is covered or not covered. Benefit coverage for health services is determined by the member-specific plan document and applicable laws that may mandate coverage for a particular service. Inclusion of a code does not imply or guarantee reimbursement or payment of a claim. Other Policies and Standards may also apply. Providers are expected to retain or have access to the necessary documentation when requested in order to support coverage.

POLICY HISTORY

Version	Date	Revision Author/Title	Summary of Changes
1	11/29/2023		New Policy