Effective Date: 12/6/2017
Last P&T Approval/Version: 04/27/2022
Next Review Due By: 04/2023
Policy Number: C10276-A

Tysabri (natalizumab)

PRODUCTS AFFECTED

Tysabri (natalizumab)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Relapsing form of multiple sclerosis (relapsing-remitting multiple sclerosis, secondary-progressive multiple sclerosis with relapses, progressive-relapsing multiple sclerosis), to include clinically isolated syndrome
Moderately to severely active Crohn’s disease

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. FOR ALL INDICATIONS:
   1. Negative anti-JCV (John Cunningham Virus) antibody test within the past 3 months OR prescriber attestation that member tested positive for JCV antibody test and member has been counseled on the higher risk of therapy causing a development of PML
      AND

2. Prescribed dose is within the FDA-approved dose range: Tysabri 300 mg IV every 4 weeks
   AND
3. Member is **NOT** receiving any other disease-modifying MS agent, immunosuppressants, or TNF inhibitors (e.g., adalimumab, infliximab)
   AND
4. Member does **NOT** have or have had progressive multifocal leukoencephalopathy (PML) and will be monitored for any new sign or symptom that may be suggestive of PML
   AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to TYSABRI (natalizumab) include: Patients who have or have had PML, Patients who have had a hypersensitivity reaction to TYSABRI]

B. MODERATE TO SEVERE ACTIVE CROHN'S DISEASE:

1. Documentation of a diagnosis of currently ACTIVE moderate to severely active Crohn's Disease(Crohn's disease activity index-CDAI score of 221-450)
   AND
2. Patient has had a trial and inadequate response (or is currently taking) corticosteroids, or corticosteroids are contraindicated in this patient AND
3. (a) Documentation patient has tried one other agent for Crohn's disease (e.g., azathioprine, 6-mercaptopurine, or methotrexate [MTX]) AND TNF-alfa agent
   OR
   (b) The patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas
   OR
   (c) The patient has had ileocolonic resection (to reduce the chance of Crohn's disease recurrence
   AND
4. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s) [DOCUMENTATIONREQUIRED]

C. MULTIPLE SCLEROSIS

1. Documentation of diagnosis of a relapsing form of multiple sclerosis as defined by the McDonald criteria (relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS, or clinically isolated syndrome)
   AND
2. (a) Documentation of **inadequate response (trial of 3 months) to ONE of the following: ONE of Interferon therapy (Avonex, Rebif, Extavia, Betaseron, Plegridy) OR Glatiramer OR Aubagio(teriflunomide), Tecfidera (dimethyl fumerate), Gilenya (fingolimod)
   **Inadequate response is defined as meeting at least TWO (2) of the following three criteria during treatment: 1) Clinical relapses (at least two relapses within the past 12 months), 2) CNS lesions progression as measured by MRI, OR 3) Worsening disability (e.g. sustained worsening of EDSS score or neurological exam findings; worsening disability include, but not limited to, decreased mobility, decreased ability to perform activities of daily living due to disease progression, or EDSS > 3.5)
   OR
   (b) Documentation member has indicators of a highly active course of multiple sclerosis: (i) age of MS onset > 40 years of age, (ii) male gender, (iii) African American, (iv) motor, sphincter, brainstem-cerebellar symptoms, (v) MRI lesions in brainstem or spina cord, OR (vi) > 2 acute relapses in first 2 years of onset with significant sustained disability following relapse

3. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s) [DOCUMENTATION REQUIRED]

CONTINUATION OF THERAPY:

A. FOR ALL INDICATIONS:

1. Negative anti-JCV (John Cunningham Virus) antibody test within the past 12 months OR prescriber attestation that member tested positive for JCV antibody test and member has been counseled on the higher risk of therapy causing a development of PML AND For continuation of therapy requests at 24 months or beyond: Documentation that member and/or caregiver has been informed about the risks of Tysabri, including that the risk of PML increases with longer treatment duration, and re-instruction on the early signs and symptoms of PML. Submit attestation of consultation for continuation of treatment.
   AND
2. Adherence to therapy at least 85% of the time as verified by prescriber and member fill history
   AND
3. Documentation of absence of unacceptable toxicity* and intolerable side effects to medication [e.g., of unacceptable toxicity include the following: hypersensitivity reactions, hepatotoxicity, signs or symptoms of PML, development of severe infections (including pneumonias, pneumocystis carinii pneumonia, pulmonary mycobacterium avium intracellular, bronchopulmonary aspergillosis, herpes, urinary tract infections, gastroenteritis, vaginitis, tonsillitis, meningitis)]

B. CROHN'S DISEASE

1. Documentation of remission of disease or improved disease activity as measured by a standardized disease activity tool (e.g., Crohn's Disease Activity Index [CDAI], Harvey Bradshaw Index [HBI], Modified Truelove and Witts Severity Index[MTWSI]).
   AND
2. Prescribed for use as monotherapy only (not prescribed for combination use with immunosuppressants or inhibitors of TNF-α)

C. MULTIPLE SCLEROSIS

1. Documentation of stabilization or positive response to Tysabri (natalizumab) treatment. Demonstrated efficacy evidenced by ANY of the following: A decrease in frequency, severity, sequelae relapses from baseline, Beneficial effect on MRI measures of disease severity, OR improvement in patient reported MS related symptoms

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Multiple Sclerosis: Board certified neurologist or Multiple sclerosis physician specialist
Crohn's Disease: Board certified gastroenterologist or colorectal surgeon, or Specialist who is consulting with a board-certified gastroenterologist or colorectal surgeon

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

One 300 mg vial every 4 weeks or 28 days

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Tysabri (natalizumab). For information on site of care, see
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous Infusion

DRUG CLASS:
Multiple Sclerosis Agents - Monoclonal Antibodies

FDA-APPROVED USES:
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
Crohn's disease (CD): For 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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Outcomes of natalizumab treatment within 3 years of relapsing-remitting multiple sclerosis diagnosis: a prespecified 2-year interim analysis of STRIVE
STRIVE is a multicenter, observational, open-label, single-arm study of natalizumab in anti–JC virus (JCV) seronegative patients with early relapsing-remitting multiple sclerosis (RRMS).

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
None

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Tysabri are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. History of or existing PML (progressive multifocal leukoencephalopathy). A woman who is trying to become pregnant, is pregnant, or is nursing. Known hypersensitivity to Tysabri or any ingredient In the formulation. Active liver disease. Medical condition that significantly compromises the immune system such as HIV infection or AIDS, leukemia, lymphoma, or organ transplantation. Active serious infections as documented in medical records. History of recurrent infections including invasive fungal infections, bacterial, viral, and other infections caused by opportunistic pathogen. Tuberculosis(active or reactivation of latent TB). Has not had a tuberculin skin test or a CDC-

recommended equivalent to rule out latent tuberculosis. Member is not up-to-date with all immunizations in agreement with current immunization guidelines prior to initiating therapy

OTHER SPECIAL CONSIDERATIONS:

Boxed Warning: Progressive multifocal leukoencephalopathy: Natalizumab increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability.
REMS program drug: Access is restricted through a REMS program called the TOUCH Prescribing Program; prescribers and pharmacies must be certified with the Tysabri Outreach Unified Commitment to Health (TOUCH) Prescribing Program.
From prescribing information: “In Crohn’s disease, TYSABRI should not be used in combination with immunosuppressants or inhibitors of TNF-α”.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J2323	injection, natalizumab, 1mg

AVAILABLE DOSAGE FORMS:
Injection: 300 mg/15 mL (20 mg/mL) solution in a single-dose vial for dilution prior to infusion

REFERENCES

1. Lichtenstein, G. R., FACG. (n.d.). Management of Crohn's Disease in Adults. Retrieved July 13,2018, from https://gi.org/guideline/management-of-crohns-disease-in-adults/
2. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline: disease-modifying therapies foradults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Available at: https://download.lww.com/wolterskluwer_vitalstream_com/PermaLink/WNL/A/WNL_2018_04 _ 19_RAEGRANT_NEUROLOGY2017835181R1_SDC3.pdf. Published April 2018.AccessedJanuary 2020.
3. Tysabri [package insert]: Cambridge, MA: Biogen Inc; December 2021
4. Terdiman JP, Gruss CB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute guideline on the use of thiopurines, methotrexate, and anti-TNF-α biologic drugs for the induction and maintenance of remission in inflammatory Crohn's disease. Gastroenterology. 2013 Dec;145(6):1459-63. doi: 10.1053/j.gastro.2013.10.047.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy	P&T QUARTER/YEAR
Q2 2022 Established tracking in new format	Historical changes on file