Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 10/03/2024

Natalizumab Products

Tyruko® (natalizumab-sztn)
Tysabri® (natalizumab)

HCPCS: Tyruko: Q5134; Tysabri: J2323

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. Diagnosis of multiple sclerosis:
      i. FDA approved age
      ii. FDA approved indication
      iii. Will not be used in combination with other disease-modifying treatments of multiple sclerosis (MS)
   b. Diagnosis of Crohn's Disease
   c. Coverage will be provided for biosimilar products for FDA labeled indications of the innovator product when criteria are met.
   d. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing.
   b. Authorization Period: One year at a time.
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Multiple Sclerosis

  - Multiple sclerosis (MS) is a chronic progressive inflammatory autoimmune disease of the central nervous system, involving axonal deterioration and demyelination. Signs and symptoms vary greatly and can include blurry or double vision, muscle weakness and stiffness, tingling in limbs, fatigue, difficulty concentrating, and many other debilitating symptoms. MS typically presents between the ages of 20 and 45, and women are affected by MS three times more frequently than men. Onset of symptoms before age 21 occurs in 3-5% of cases and is considered juvenile MS.

  - Several clinical presentations of MS have been identified including relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), primary progressive MS (PPMS), and a rare form called progressive-relapsing (PRMS). All forms of MS are associated with neurologic dysfunction. Relapsing-remitting MS affects the majority of newly diagnosed individuals and about half of the people diagnosed with RRMS will transition to SPMS within 10-20 years of initial diagnosis. Relapses are characterized as periods of sudden worsening of symptoms or new symptoms. Often, the periods of remission between relapses will last weeks, months, or even years.

  - Patients diagnosed with PPMS experience continued and gradual physical decline without remissions. PPMS affects as many men as women and typically presents after the age of 40. PRMS affects only about 5% of patients diagnosed with MS and is characterized by steady worsening dysfunction with distinct exacerbations.

  - The American Academy of Neurology (AAN) 2018 treatment guidelines for adults with MS state that there are a variety of disease modifying therapies (DMTs) available; therefore, evaluating patient preference may improve acceptance and adherence to DMT. Considerations when choosing DMT include safety, route of administration, lifestyle, cost, efficacy, common adverse effects, tolerability, comorbid conditions, and concomitant medications. Recommendations for first-line therapy are not specified, with the exception of Lemtrada (alemtuzumab), Tysabri (natalizumab), and Gilenya® (fingolimod) for highly active MS and Ocrevus (ocrelizumab) for primary progressive MS.

  - There are no formal guidelines for the treatment of pediatric MS which is rare. Less than 5,000 children and teens are living with MS in the United States. Pediatric patients with MS typically experience more frequent relapses compared to adults with MS but recover from relapses more quickly than adults. Although Gilenya and Tascenso ODT are the only approved therapies for pediatric MS, many of the disease modifying therapies prescribed for adults with MS are also prescribed for pediatric MS based on supporting data such as small retrospective studies and case studies.

- Crohn's Disease

  - Natalizumab is a monoclonal antibody indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's Disease (CD) with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of tumor necrosis factor alpha (TNF-α). Natalizumab is also indicated for multiple sclerosis and that indication is addressed in a the Multiple Sclerosis Disease Modifying Agents Policy. Natalizumab is available as the innovator product, Tysabri, as well as a biosimilar product Tyruko.

  - Natalizumab is not recommended as a first-line option due to potentially serious safety concerns, specifically progressive multi focal leukoencephalopathy (PML). PML is a viral infection of the brain that usually leads to death or severe disability. The risk of PML increase with the number of infusions received. Risk factors for

the development of PML include the presence of anti-JCV 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 with natalizumab.

- Other disease modifying CD treatments currently include, but are not limited to Humira® (adalimumab), Remicade® (infliximab), Cimzia® (certolizumab), Entyvio® (vedolizumab), and Stelara® (ustekinumab).

- No studies have shown that the efficacy of natalizumab is superior to other disease modifying therapies in the treatment of CD.

References:

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3. The Regence Group. Medical Policy for Tysabri.
4. Goodin DS, Cohen BA, et al. Assessment: The use of natalizumab (Tysabri) for the treatment of multiple sclerosis. Report of the therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2008;71:766-773.
5. Polman CH, O'connor PW, Havrdova E, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. N England J Med. Mar 2006 2;354(9):899-910.
6. Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018 Apr;113(4):481-517.
7. U.S. Food and Drug Administration Drug Safety Communication: Safety Update on Progressive Multifocal Encephalopathy (PML) associated with Tysabri (natalizumab). http://www.fda.gov/Drugs?drugSafety/ucm252045.htm. Accessed Aug 1, 2014
8. Tyruko [prescribing information]. Princeton, NJ: Sandoz, Inc.; August 2023
9. IPD Analytics. Clinical Pipeline. Accessed August 19, 2024. http://www.ipdanalytics.com
10. Drug Facts and Comaprisons. eFacts (online). 2022. Available from Wolters Kluwer Health, Inc. Accessed January 3, 2023.
11. 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 at: https://n.neurology.org/content/neurology/90/17/777.full.pdf. Accessed on January 3, 2023.
12. Lotze TE. Treatment and prognosis of pediatric multiple sclerosis. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on January 3, 2023).
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14. IPD Analytics. Payer & Provider Insights. January 2022. Accessed January 3, 2023. https://www.ipdanalytics.com

Policy History		
#	Date	Change Description
3.3	Effective Date: 10/03/2024	Annual review of criteria was preformed. No updated criteria at this time.
3.2	Effective Date: 10/12/2023	Renamed to Natalizumab products policy and updated policy to include Tyruko
3.1	Effective Date: 09/14/2023	UM medical management system update for BCBSM and BCN for Tyruko
3.0	Effective Date: 08/10/2023	Annual review of criteria was performed. No changes made to the criteria at this time.

2.9	Effective Date: 02/02/2023	Updated policy to include Briumvi
2.8	Effective Date: 10/06/2022	Added Mavenclad and generic Copaxone back to policy
2.7	Effective Date: 08/04/2022	Annual review of criteria was performed, no changes were made
2.6	Effective Date: 02/10/2022	Added Tascenso to the policy
2.5	Effective Date: 08/12/2021	Annual review of criteria was performed. Updated renewal criteria to include our standard renewal criteria
2.4	Effective Date: 06/10/2021	Added Ponvory to the policy and removed prescriber requirement.
2.3	Effective Date: 10/08/2020	Added Kesimpta to the policy
2.2	Effective Date: 08/13/2020	Annual review of criteria was performed, no changes were made
2.1	Effective Date: 10/01/2019	UM medical management system update for BCBSM and BCN for Tysabri
2.0	Effective Date: 08/15/2019	Updated criteria to list indication only and include the trial and failure of preferred products statement After MBDC: Removed investigational use sections from drug specific criteria due to updated indications for many MS medications
1.9	Effective Date: 02/14/2019	Updated Lemtrada quantity limit
1.8	Effective Date: 08/09/2018	Annual review of criteria was performed, no changes were made
1.7	Effective Date: 07/01/2018	UM medical management system update for BCBS for Tysabri
1.6	Effective Date: 08/10/2017	Updated step therapy
1.5	Effective Date: 11/10/2016	Updated wording of indication
1.4	Effective Date: 08/11/2016	Updated MD attestation
1.3	Effective Date: 01/01/2016	Document updated with specified drugs required
1.2	Effective Date: 08/13/2015	Aligned Tysabri criteria with other MS drugs
1.1	Effective Date: 01/01/2015	UM medical management system update for BCBS for Tysabri
1.0	Effective Date: 10/30/2014	Updated criteria to require a neurologist or gastroenterologist, anti-JVC testing, and updated initial authorization to 6 months only, added criteria for continuation of coverage

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form

Blue Cross Blue Shield Blue Care Network of Michigan

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This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for: ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
2. Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
3. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #4) *Reason for Hospital Outpatient administration:* _____
   ☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
4. Please specify location of administration if hospital outpatient infusion: _____
5. Please specify location of administration if hospital inpatient infusion: _____
6. Please provide the NPI number for the place of administration: _____
7. **Initiation AND Continuation of therapy:**
   a. What is the patient's diagnosis? _____
   b. What other medication has the patient received for their condition? Please list_____
      i. Please describe the response to previous therapies:
      _____
   c. Will the patient be receiving any other treatment for the listed condition while on this medication? Please list:
      _____
   d. Please list any labs values important for diagnosing or monitoring this patient's condition:
      _____
8. **Continuation of therapy:**
   a. Has the patient progressed while on this medication? ☐ yes ☐ no
   b. How has the patient's condition changed while on this medication?
      ☐ Improved: Please describe: _____
      ☐ Stable: please describe: _____
      ☐ Worsened; Please describe: _____
      ☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review **(required)**

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021