BlueCross BlueShield of North Carolina

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Corporate Medical Policy

Natalizumab (Tysabri®)

File Name:	natalizumab_tysabri
Origination:	11/2010
Last CAP Review:	5/2019
Next CAP Review:	5/2020
Last Review:	5/2019

Description of Procedure or Service

Natalizumab is an integrin-4 receptor antagonist labeled for the treatment of Multiple Sclerosis (MS) and Crohn's Disease (CD). Natalizumab is a recombinant humanized immunoglobulin-4 monoclonal antibody directed against the integrin alpha-4 adhesion molecule. It is the first medication of this type in a new class of selective adhesion molecule inhibitors.

Natalizumab binds to the alpha-4 subunit of integrins alpha-4-beta-1 and alpha-4-beta-7 expressed on the surface of leukocytes (except neutrophils). Integrin alpha-4-beta-7 binds to the mucosal vascular addressin cell adhesion molecule-1 (MadCam-1) in the gastrointestinal endothelium. When natalizumab binds to alpha-4 integrins, it disrupts integrin interaction with MadCam-1, preventing the passage of leukocytes into the gut.

Multiple Sclerosis
Monotherapy for the treatment of patients with relapsing forms of multiple sclerosis to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations. The efficacy of Tysabri beyond two years is unknown. Because Tysabri increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability, Tysabri is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate multiple sclerosis therapy. Safety and efficacy in patients with chronic progressive multiple sclerosis have not been established.

Crohn's Disease
Induction and maintenance of 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 Crohn's disease therapies **and** TNF-α inhibitors. Tysabri should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for natalizumab (Tysabri) for the treatment of multiple sclerosis and Crohn's disease when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit

design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Natalizumab (Tysabri) is covered

Natalizumab (Tysabri) may be considered medically necessary for patients:

1. 18 years of age or older;

2. Who are not significantly immunocompromised;

3. Who have one of the following conditions:

   A. Relapsing form of Multiple Sclerosis, with an inadequate response to, or are unable to tolerate at least one alternate multiple sclerosis disease-modifying therapy (Betaseron®, Extavia®, Avonex®, Rebif®, Copaxone®, Aubagio®, Tecfidera™, or Gilenya®), or has had a particularly aggressive initial disease course; **AND**

   The patient is not receiving combination therapy of natalizumab (Tysabri) with any other disease-modifying drug(s) for multiple sclerosis, or in combination with any other chronic immunosuppressive therapy.

   B. Moderate to severe Crohn's Disease, with an inadequate response to a trial of at least one of the following agents:

   1.) Corticosteroids
   2.) 5-aminosalicylates (e.g., sulfasalazine, Asulfidine, Asacol, Pentasa, Dipentum, Colazal)
   3.) 6-mercaptopurine, azathioprine (Imuran), metronidazole, and/or methotrexate (MTX); **AND**

   Patient has had an inadequate response to, or is unable to tolerate, treatment with at least one TNF-a inhibitor: adalimumab (Humira), certolizumab pegol (Cimzia), or infliximab (Remicade); **AND**

   Patient will not receive combination therapy of natalizumab (Tysabri) with TNF-a inhibitor therapy (e.g., Humira, Remicade, Cimzia), **OR** concurrent therapy with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate).

When Natalizumab (Tysabri) is not covered

Natalizumab (Tysabri) is considered **investigational** for all other indications including but not limited to non-relapsing MS, primary progressive MS, rheumatoid arthritis, or ulcerative colitis.

Policy Guidelines

Only prescribers registered in the MS TOUCH® Prescribing Program may prescribe Tysabri for multiple sclerosis. The recommended dose of Tysabri for multiple sclerosis is 300 mg intravenous infusion over one hour every four weeks.

Only prescribers registered in the CD TOUCH® Prescribing Program may prescribe Tysabri for Crohn's disease. The recommended dose of Tysabri for Crohn's disease is 300 mg intravenous infusion over one hour every four weeks.

Tysabri should not be used with concomitant immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or concomitant inhibitors of TNF-α. Aminosalicylates may be continued during treatment with Tysabri.

Site of Care Eligibility

1. Natalizumab administration may be given in an inpatient setting if the inpatient setting is medically necessary. An inpatient admission for the sole purpose of natalizumab infusion is not medically necessary, OR
2. Natalizumab administration in a hospital outpatient setting is considered medically necessary if the following criteria are met:
    a. History of mild adverse events that have not been successfully managed through mild pre-medication (diphenhydramine, acetaminophen, steroids, fluids, etc.), OR
    b. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity, OR
    c. First infusion, OR
    d. Less than 3 months since first natalizumab infusion, OR
    e. First infusion after six months of no natalizumab infusions, OR
    f. Requirement of a change in natalizumab product.
3. Members who do not meet the criteria above are appropriate for natalizumab administration in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional. Inpatient and hospital outpatient infusion, in the absence of the criteria in #1 or #2 above is considered not medically necessary.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: *J2323, 86711*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

U.S. Food and Drug Administration (FDA). Tysabri (natalizumab) injection. Highlights of prescribing information. Rockville, MD: FDA; January 2008. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/125104s033lbl.pdf.

U.S. Food and Drug Administration. http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2006/125104s015LTR.pdf

Tysabri (natalizumab). Product information. Biogen Idec, Inc. 2010

Specialty Matched Consultant Advisory Panel – 5/2011

National Institute for Health and Clinical Excellence (NICE). Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis. NICE Technology Appraisal Guidance 127. Retrieved 3/26/2012 from http://www.nice.org.uk/nicemedia/live/11822/36136/36136.pdf.

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U.S. Food And Drug Administration. FDA Drug Safety Communication: New risk factor for Progressive Multifocal Leukoencephalopathy (PML) associated with Tysabri (natalizumab). Retrieved 4/9/2013 from http://www.fda.gov/Drugs/DrugSafety/ucm288186.htm

Bloomingren G, et al. Risk of natalizumab-associated progressive multifocal leukoencephalopathy. N Engl J Med 2012; 366:1870-1880

Specialty Matched Consultant Advisory Panel – 5/2013

Specialty Matched Consultant Advisory Panel – 5/2014

Tysabri (natalizumab). Prescribing information. Biogen Idec, Inc. December 2013.

Specialty Matched Consultant Advisory Panel – 5/27/15

Tysabri (natalizumab). Prescribing information. Biogen Idec, Inc. May 2015.

Specialty Matched Consultant Advisory Panel – 5/25/16

Tysabri (natalizumab). Prescribing information. Biogen Idec, Inc. May 2016.

Specialty Matched Consultant Advisory Panel – 5/31/17

Specialty Matched Consultant Advisory Panel – 5/23/18

Specialty Matched Consultant Advisory Panel – 5/15/19

Policy Implementation/Update Information

1/1/2011 New medical policy issued. Natalizumab (Tysabri) may be considered medically necessary for the treatment of multiple sclerosis and Crohn's disease when the medical criteria and guidelines are met. Notification date 1/1/2011 for effective date 4/1/2011. (lpr)

6/21/11 Specialty Matched Consultant Advisory Panel review 5/25/2011. No change to policy statement. (btw)

7/24/12 Specialty Matched Consultant Advisory Panel review 5/16/2012. No change to policy statement. References added. (btw)

12/28/12 New 2013 code, 86711 added to Billing/Coding section. (btw)

7/1/13 Specialty Matched Consultant Advisory Panel review 5/15/2013. No change to policy statement. References added. (btw)

7/30/13 Added "Aubagio® and Tecfidera™ "to 3.A. Relapsing form of Multiple Sclerosis, in the When Covered section based on CAP review. (btw)

6/10/14 Specialty Matched Consultant Advisory Panel review 5/27/14. No change to policy statement. (btw)

7/28/15 Reference added. Specialty Matched Consultant Advisory Panel review 5/27/15. (sk)

7/1/16	Specialty Matched Consultant Advisory Panel review 5/25/16. (sk)
6/30/17	Reference added. Specialty Matched Consultant Advisory Panel review 5/31/17. (sk)
12/29/17	Site of care criteria added to Policy Guidelines. Policy notification given 12/29/17 for effective date 4/1/2018. (sk)
6/8/18	Specialty Matched Consultant Advisory Panel review 5/23/18. No change to policy intent. (krc)
5/28/19	Specialty Matched Consultant Advisory Panel review 5/15/19. No change to policy intent. (krc)