Clinical Policy: Natalizumab (Tysabri)

Reference Number: PA.CP.PHAR.259
Effective Date: 01/18
Last Review Date: 07/17

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for natalizumab (Tysabri®).

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness® that Tysabri is **medically necessary** for the following indications:

I. Initial Approval Criteria

A. Multiple Sclerosis (must meet all):

1. Diagnosis of a relapsing form of multiple sclerosis (MS);
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Failure of one of the following (a or b) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced:
   a. Tecfidera or Gilenya and any of the following: an interferon-beta agent *(Avonex and Plegridy are preferred agents)*, or glatiramer *(Glatopa 20 mg and Copaxone 40 mg are preferred agents)*;
   b. Tecfidera and Gilenya;
5. Member will not use other disease modifying therapies for MS concurrently;
6. Dose does not exceed 300 mg every 4 weeks (1 vial every 4 weeks).

Approval duration: 6 months

B. Crohn's Disease (must meet all):

1. Diagnosis of Crohn's disease (CD) and (a or b):
   a. Member is identified as moderate/high risk based on one of the following:
      i. Age at initial diagnosis < 30 years;
      ii. Extensive anatomic involvement (e.g., ileocecal disease, continuous ileocolonic disease, small bowel disease);
      iii. Perianal and/or severe rectal disease;
      iv. Deep ulcers;
      v. Prior surgical resection;
      vi. Stricturing and/or penetrating behavior;
   b. Failure of an immunomodulator (e.g., azathioprine, 6-mercaptopurine (6MP), methotrexate (MTX)], used for ≥ 3 months unless contraindicated or clinically significant adverse effects are experienced;
2. Failure of adalimumab (*Humira is preferred)* AND one other tumor-necrosis factor (TNF) α inhibitor (i.e., infliximab, Cimzia) each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for adalimumab and all TNFα inhibitors*

3. Prescribed by or in consultation with a gastroenterologist;
4. Age ≥ 18 years;
5. Immunosuppressants (e.g., azathioprine, cyclosporine, 6-MP, MTX) or TNF-α inhibitors will not be administered concurrently – aminosalicylates may be continued;
6. Prescribed dose does not exceed 300 mg every 4 weeks.

Approval duration: 6 months

C. Other diagnoses/indications: Refer to PA.CP.PHAR.57 - Global Biopharm Policy

II. Continued Approval

A. Multiple Sclerosis (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (e.g., improved or maintained disease control evidenced by decreased or stabilized Expanded Disability Status Scale score or reduction in relapses or magnetic resonance imaging lesions);
3. Member is not using other disease modifying therapies for MS concurrently;
4. If request is for a dose increase, new dose does not exceed 300 mg every 4 weeks (1 vial every 4 weeks).

Approval duration: 12 months

B. Crohn's Disease (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Responding positively to therapy;
3. Immunosuppressants (e.g., azathioprine, cyclosporine, 6-MP, MTX) or TNF-α inhibitors will not be administered concurrently – aminosalicylates may be continued;
4. Prescribed regimen does not exceed 300 mg every 4 weeks.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy**.**

Background

Description/Mechanism of Action:

Tysabri is a recombinant humanized IgG4κ monoclonal antibody produced in murine myeloma cells. It binds to the α4-subunit of α4β1 and α4β7 integrins expressed on the surface of all

leukocytes except neutrophils, and inhibits the α4-mediated adhesion of leukocytes to their counter-receptor(s). The specific mechanism(s) by which Tysabri exerts its effects in multiple sclerosis and Crohn's disease have not been fully defined.

- In multiple sclerosis, the clinical effect of natalizumab may be secondary to blockade of the molecular interaction of α4β1-integrin expressed by inflammatory cells with vascular cell adhesion molecule-1 on vascular endothelial cells, and with connecting segment-1 and/or osteopontin expressed by parenchymal cells in the brain.
- In Crohn's disease, the clinical effect of natalizumab may be secondary to blockade of the molecular interaction of the α4ß7-integrin receptor with mucosal addressin cell adhesion molecule-1 expressed on the venular endothelium at inflammatory foci. The interaction of the α4β7 integrin with the endothelial receptor mucosal addressin cell adhesion molecule-has been implicated as an important contributor to the chronic inflammation that is a hallmark of the disease.

Formulations:
Tysabri is supplied as 300 mg natalizumab in 15 mL in a sterile, single-use vial free of preservatives.

FDA Approved Indication(s):
Tysabri is an integrin receptor antagonist/intravenous infusion indicated for:

- Treatment of patients with relapsing forms of multiple sclerosis.
- Inducing and maintaining clinical response and remission in adult patients with moderately to severely active CD with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of (TNF-α).

Limitations of use:

- Tysabri increases the risk of progressive multifocal leukoencephalopathy . When initiating and continuing treatment with Tysabri, physicians should consider whether the expected benefit of Tysabri is sufficient to offset this risk.
- In CD, Tysabri should not be used in combination with immunosuppressants or inhibitors of TNF-α.

Appendices
Appendix A: Abbreviation Key
6-MP: 6-mercaptopurine
CD: Crohn's disease
FDA: Food and Drug Administration
MS: multiple sclerosis
MTX: methotrexate
RRMS: relapsing-remitting multiple sclerosis
TNF-α: tumor-necrosis factor-α

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2323	Injection, natalizumab, 1 mg

Reviews, Revisions, and Approvals	Date	Approval Date

References

1. Tysabri Prescribing Information. Cambridge, MA: Biogen Inc; May 2016. Available at http://www.tysabri.com. Accessed June 14, 2017.
2. Costello K, Halper J, Kalb R, Skutnik L, Rapp R. The use of disease-modifying therapies in multiple sclerosis, principles and current evidence – a consensus paper by the Multiple Sclerosis Coalition. July 2016. Accessed June 13, 2017.
3. Olek MJ. Disease-modifying treatment of relapsing-remitting multiple sclerosis. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at www.UpToDate.com. Accessed June 13, 2017.
4. Olek MJ. Diagnosis of multiple sclerosis in adults. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at www.UpToDate.com. Accessed June 13, 2017.
5. Lichtenstein GR, Hanauer SB, Sandborn WJ, and the Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol. 2009;104(2):465-483.
6. Sandborn WJ. Crohn's Disease Evaluation and Treatment: Clinical Decision Tool. Gastroenterology 2014; 147: 702-705.
7. Bernell O, Lapidus A, Hellers G. Risk Factors for Surgery and Postoperative Recurrence in Crohn's Disease. Annals of Surgery. 2000; 231(1): 38-45.