

<b>Policy Title:</b>	Tysbari (natalizumab) (Intravenous)		
000576	000576	<b>Department:</b>	PHA
<b>Effective Date:</b>	09/12/2018		
<b>Review Date:</b>	//		
<b>Revision Date:</b>	//		

**Purpose:** To support safe, effective and appropriate use of Tysbari (natalizumab) in the treatment of Multiple Sclerosis and Crohn’s disease.

**Scope:** Medicaid, Exchange, MMP

**Policy Statement:**

Tysbari (natalizumab) is covered under the medical benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

**Procedure:**

Coverage of Tysbari (natalizumab) will be reviewed prospectively via the prior authorization process based on criteria below.

**Initial Criteria Coverage:**

- Patient is at least 18 years of age; and
- Patient has had anti-JCV antibody testing with ELISA prior to initiating treatment with natalizumab and annually thereafter; and
- Cannot be used in combination with antineoplastic, immunosuppressant, or immunomodulating agents; and
- Patient must not have a systemic medical condition resulting in significantly compromised immune system function; and

Multiple Sclerosis:

- Patient is diagnosed with a relapsing form of multiple sclerosis and documented by laboratory report (i.e. MRI); and
  - Member has failed, demonstrated intolerance, or is contraindicated to at least two drugs indicated for the treatment of relapsing MS
- Must be prescribed by a neurologist; and
- Used as monotherapy for the treatment of relapsing forms of MS
- Dose does not exceed 300mg( 300 billable units) every 28 days

Crohn's Disease:

- Patient is diagnosed with Crohn's disease by a gastroenterologist; and
- Prescriber has assessed baseline disease severity utilizing an objective measure/tool; and
- Patient has had failure, intolerance, or contraindication to at least two oral immunosuppressive therapy for at least 3 months, such as corticosteroids, methotrexate, azathioprine, and/or 6-mercaptopurine; and
- Patient has had failure, intolerance, or contraindication to at least one TNF-Inhibitor therapy for at least 3 months, such as infliximab, certolizumab, or adalimumab; and
- Patient is not taking in combination with another biologic drug or immunosuppressant (e.g., 6-mercaptopurine, azathioprine, cyclosporine, methotrexate, etc) used for Crohn's disease.

***Continuation of therapy:***

- Continuation of therapy criteria for MS:
  - Patient is tolerating treatment
  - Dose does not exceed 300mg( 300 billable units) every 28 days
  - Patient has annual anti-JCV antibody testing with ELISA
  - Patient has experienced disease improvement or slowing of disease worsening (eg, no decline in Expanded Disability Status Score [EDSS] or MRI findings) since initiating therapy.
- Continuation of therapy criteria Crohn's disease:
  - Patient is tolerating treatment
  - Patient has annual anti-JCV antibody testing with ELISA
  - Dose does not exceed 300mg( 300 billable units) every 28 days
  - For initial renewal only:
    - patient must show clinical response and remission of disease is seen by 12 weeks
  - For all subsequent renewals:
    - Patient does not require additional steroid use that exceeds three months in a calendar year
    - Disease response as indicated by improvement in signs and symptoms compared to baseline such as endoscopic activity, number of liquid stools, presence and severity of abdominal pain, presence of abdominal mass, body weight compared to IBW, hematocrit, presence of extra intestinal complications, use of anti-diarrheal drugs, and/or an improvement on a disease activity scoring tool [e.g. an improvement on the Crohn's Disease Activity Index (CDAI) score or the Harvey-Bradshaw Index score.]

**Coverage durations:**

- Initial coverage criteria = 3 months for Crohn's disease and 6 months for MS
  - Continuation of therapy = 6 months
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**Investigational use:** All Multiple sclerosis therapies is considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in one of the above listed resources. Neighborhood does not provide coverage for drugs when used for investigational purposes.

**Additional information:**

Indications:

- Tysabri(natalizumab) is FDA approved as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis and indicated 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- $\alpha$ .

**Limitation of Use:**

- Tysabri (natalizumab): Increases the risk of PML and should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF- $\alpha$

**Dosing:**

- The recommended dose of Tysabri\_(natalizumab) for MS or Crohn's disease is 300mg via IV infusion every 4 weeks and if the patient with Crohn's disease has not experienced therapeutic benefit by 12 weeks of induction therapy, discontinue use.

**Administration:**

- Under the close supervision of an experienced healthcare professional with access to appropriate medical support to manage severe reactions such as serious infusion reactions.

### Applicable Codes:

Below is a list of billing codes applicable to covered treatment options for multiple sclerosis. The below tables are provided for reference purposes and may not be all inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria are provided in the procedure section.

### Codes:

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis(specify substance or drug), initial, up to 1 hour
96366	Intravenous infusion ,Each additional hour
J2323	Injection,natalizumab, 1mg

### References:

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2. Fox RJ, Cutter G, Chan A, et al. Comparative Effectiveness Using A Matching-Adjusted Indirect Comparison Between Delayed-Release Dimethyl Fumarate and Fingolimod for The Treatment of Relapsing-Remitting Multiple Sclerosis. *Value Health.* 2015 Nov;18(7):A750. Epub 2015 Oct 20. [PubMed](#)
3. Metin H, Huppertz H. Adjusted Indirect Comparison of Oral Multiple Sclerosis Agents. *Value Health.* 2015 Nov;18(7):A750. Epub 2015 Oct 20. [PubMed](#)
4. Tramacere I, Del Giovane C, Salanti G, et al. Immunomodulators and immunosuppressants for relapsing-remitting multiple sclerosis: a network meta-analysis. *Cochrane Database Syst Rev.* 2015. [PubMed](#)
5. Tolley K, Hutchinson M, You X, et al. A Network Meta-Analysis of Efficacy and Evaluation of Safety of Subcutaneous Pegylated Interferon Beta-1a versus Other Injectable Therapies for the Treatment of Relapsing-Remitting Multiple Sclerosis. *PLoS One.* 2015;10(6):e0127960.
6. Bainbridge JL, Miravalle A, Corboy JR. Multiple Sclerosis. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L, eds. *Pharmacotherapy: A Pathophysiologic Approach.* 9th ed. New York, NY: McGraw-Hill; 2014. <http://accesspharmacy.mhmedical.com/content.aspx?bookid=689&Sectionid=45310489>. Accessed May 18, 2016.
7. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology.* 2002;58(2):169-178.
8. Hauser SL, Bar-Or A, Comi G, Giovannoni G, Hartung HP, Hemmer B, Lublin F, Montalban X, Rammohan KW, Selmaj K, et al. Ocrevus versus Interferon Beta-1a in Relapsing Multiple Sclerosis. *N Eng J Med.* 2016;376(3):221–234. doi: 10.1056/NEJMoa1601277.
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10. Tysabri prescribing information. South San Francisco, CA: Elan Pharmaceuticals, Inc.; 2018 July.