

Title: natalizumab (Tysabri)

Origination: 08/26/09	Revised:	Annual Review: 12/15/11
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Purpose:

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

Background Information:

Reference Statement

- Guidelines will be compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.

Medication Summary

- Natalizumab (Tysabri) is a human monoclonal antibody that binds to, and inhibits, alpha-4 integrins from adhering to their counter-receptors. This inhibition prevents T-lymphocytes from passing through the blood brain barrier, thus impeding the demyelinating process of multiple sclerosis (MS). Tysabri also attenuates T-cell mediated intestinal inflammation.
- Natalizumab is indicated for use as monotherapy treatment for relapsing forms of multiple sclerosis. Because Tysabri increases the risk of progressive multifocal leukoencephalopathy (PML), its use is recommended for Members who have had an inadequate response to, or are unable to tolerate, other therapies for multiple sclerosis (MS).
- Natalizumab is also indicated for the treatment of moderately to severely active Crohn's disease in Members who have had an inadequate response to, or are unable to tolerate, conventional therapies as well as TNF modifiers (such as Humira, Remicade).
- Natalizumab is available only through a restricted distribution program, called the TOUCH (Tysabri Outreach Unified Commitment to Health) Prescribing Program, in an attempt to identify cases of PML. Under this program, only prescribers and Members registered with the program are able to prescribe, administer, and receive the medication. Treatment must be reauthorized every six (6) months.
- Natalizumab is administered as a 300mg IV infusion over one (1) hour every four (4) weeks, and is available as a 300mg/15ml solution.

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Background Information, continued:

Eligibility Criteria

- Member must be eligible and have applicable benefits.
- Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.

Exclusions

- Current or history of progressive multifocal leukoencephalopathy (PML).
- Member less than 18 years of age, as safety and efficacy have not been established in children or adolescents.

Procedure:

- 1.0 Request for *initial therapy* for **multiple sclerosis (MS)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
 - 1.1 Provider must be a neurologist; **AND**
 - 1.2 Diagnosis of relapsing MS (RMS) or relapsing-remitting MS (RRMS); **AND**
 - 1.3 Member has had an inadequate response (as demonstrated by continued disease activity measured clinically or by MRI) and/or intolerance to **all of the following** medications:
 - 1.3.1 Avonex or Rebif;
 - 1.3.2 Betaseron;
 - 1.3.3 Copaxone;
 - 1.4 If the Member meets the above criteria, initial therapy may be approved for up to three (3) months at a dose of 300 mg every four (4) weeks.
- 2.0 Request for *continuation of therapy* beyond the initial authorization period for **multiple sclerosis (MS)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying a reduction in the Member's signs and symptoms of MS (measured clinically or by MRI):
 - 2.1 If the Member meets the above criteria, continuation of therapy may be approved for up to six (6) months at a dose of 300 mg every four (4) weeks.

Procedure, continued:

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3.0 Request for *initial therapy* for **Crohn's disease** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:

3.1 Provider must be a gastroenterologist; **AND**

3.2 Diagnosis of moderately to severely active Crohn's disease as evidenced by:

3.2.1 Radiological or endoscopic confirmation; **AND**

3.2.2 **At least one (1)** of the following more prominent symptoms:

3.2.2.1 Fevers;

3.2.2.1 Significant weight loss;

3.2.2.1 Abdominal pain or tenderness;

3.2.2.1 Intermittent nausea or vomiting (without obstructive findings);

3.2.2.1 Significant anemia;

3.2.2.1 Diarrhea;

OR

3.2.2 Crohn's disease Activity Index (CDAI) score of 220-450 points;

AND

3.3 Member shows inadequate response to a three (3) to six (6) month minimum trial of **OR** is not a candidate for at least **two (2)** of the following medications:

3.3.1 mesalamine (Asacol, Lialda, Pentasa, Rowasa, Canasa);

3.3.2 sulfasalazine (Azulfidine);

3.3.3 corticosteroids (prednisone, methylprednisolone, budesonide, Entocort);

3.3.4 azathioprine (Imuran);

3.3.5 mercaptopurine (6-MP);

3.3.6 methotrexate;

AND

3.4 Member shows inadequate response to a three (3) to six (6) month minimum trial of an adequate dose of, **OR** is not a candidate for, **both** of the following TNF modifiers:

3.4.1 Remicade (infliximab); **AND**

3.4.2 Humira (adalimumab);

3.5 If the Member meets all of the above criteria, initial therapy may be approved for up to three (3) months at a dose of 300 mg every four (4) weeks.

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Procedure, continued:

- 4.0 Request for *continuation of therapy* beyond the initial authorization period for **Crohn's disease** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying a reduction in the Member's signs and symptoms of Crohn's disease:
- 4.1 If the Member meets all the above criteria, continuation of therapy may be approved for up to six (6) months at a dose of 300 mg every four (4) weeks.

References:

1. Kappos, L et al. "Natalizumab treatment for multiple sclerosis: recommendations for patient selection and monitoring." *The Lancet Neurology* – Vol 6, Issue 5 (May 2007).
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2008. Available at: <http://cp.gsm.com>.
3. "Tysabri Risk Minimization Action Plan: Summary of TOUCH." *Department of Health & Human Services*. Public Health Service. Food and Drug Administration.
4. Farrel, Richard J et al. "Medical management of Crohn's disease in adults". Up To Date Online [serial on the Internet]. 2009 August. Available from: <http://www.uptodate.com/patients/content/topic.do?topicKey=~sFsaDtdCNXv/4q>
5. *Tysabri* (natalizumab) Full Prescribing Information and Medication Guide. Elan Pharmaceuticals, Inc., South San Francisco, CA 94080.
6. Goodin, DS et al. "Assessment: the use of natalizumab (Tysabri) for the treatment of multiple sclerosis (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology." *Neurology* Sep 2008.
7. Sandborn, William J. "Biologics Should Be Used Early in the Treatment of Crohn's Disease". *American Gastroenterological Association*. June/July 2006.

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Disclaimer Information:

Prior Authorization criteria are developed to determine coverage for AvMed Health Plans' benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. AvMed Health Plans makes coverage decisions based on the Member's benefit plan contract and these criteria. This guideline sets forth concise clinical coverage criteria which have been developed from a review of current literature, policies of the FDA and other government agencies, and other appropriate references, in consultation and with approval from practicing physicians who are members of AvMed's Pharmacy and Therapeutic committee. Treating providers are solely responsible for the medical advice and treatment of Members. This guideline may be updated and therefore is subject to change. The use of these criteria is neither a guarantee of payment nor a final prediction of how specific claim(s) will be adjudicated.