

Origination Date: 3/07	Revision Date(s): 3/08, 3/09
Developed By: Medical Criteria Committee	

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Approved: Robert Neal Mills MD Date: 03/16/09

ODS Rx <sup>1.0</sup> <input type="checkbox"/>	ODS Rx <sup>2.0</sup> <input checked="" type="checkbox"/>	OEBB <input checked="" type="checkbox"/>	OHP <input type="checkbox"/>
NON-SPECIALTY <input type="checkbox"/>	SPECIALTY <input checked="" type="checkbox"/>		
PA <input checked="" type="checkbox"/>	QLL <input type="checkbox"/>	STEP THERAPY <input type="checkbox"/>	

## Natalizumab (Tysabri®)

**PURPOSE:** To ensure the appropriate use of Tysabri®.

**QUANTITY LIMIT:**

- 15 mL (1 vial) per 30 days

**STANDARD DOSING:**

- Multiple Sclerosis: 300 mg infused via IV over 1 hour every 4 weeks
- Chron's Disease: 300 mg infused via IV over 1 hour every 4 weeks

**DESCRIPTION:** Tysabri is a monoclonal antibody to the alpha-4 subunit of integrin molecules which are important to adhesion and migration of cells from the vasculature into inflamed tissue. Tysabri blocks integrin association with vascular receptors, limiting adhesion and transmigration of leukocytes. Efficacy may be related to the blockade of T-lymphocyte migration into the central nervous system.

**PRODUCT AVAILABILITY:**

Natalizumab (Tysabri)

- 300 mg as an injection, solution, concentrate, single-use 15 mL vial.

**INDICATIONS:**

Crohn disease (adults):

- For inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional Crohn disease therapies and inhibitors of tumor necrosis factor alpha (TNF- $\alpha$ ). Do not administer natalizumab in combination with immunosuppressants (eg, azathioprine, cyclosporine, methotrexate, 6-mercaptopurine) or inhibitors of TNF- $\alpha$ .

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Multiple sclerosis (MS) (adults):

- As 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 safety and efficacy of natalizumab beyond 2 years are unknown.
- Because natalizumab increases the risk of PML, an opportunistic viral infection of the brain that usually leads to death or severe disability, natalizumab is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, alternative multiple sclerosis therapies.
- Safety and efficacy in patients with chronic progressive multiple sclerosis have not been established.

**POLICY:**

- Grandfathering is allowed when an enrollee has a claim for Tysabri® within the previous 180 days.

**GUIDELINES FOR USE:**

- 1) **Is the patient over 18 years of age?**
  - a. If yes, to #2
  - b. If no, forward to clinical
- 2) **Has the patient experienced progressive multifocal leukoencephalopathy?**
  - a. If yes, forward to clinical for review
  - b. If no, go to #3
- 3) **Does the patient have a diagnosis of Multiple Sclerosis?**
  - a. If yes, go to #4
  - b. If no, go to #6
- 4) **Did the patient have an inadequate response to, or was unable to tolerate treatment with Copaxone or interferon (e.g. Avonex, Betaseron, Rebif)?**
  - a. If yes, go to #5
  - b. If no, forward to clinical for review
- 5) **Will the patient be taking Tysabri with Copaxone or interferon (e.g. Avonex, Betaseron, Rebif)?**
  - a. If yes, forward to clinical for review
  - b. If no, go to #12
- 6) **Is the patient being treated for moderate-to-severe Crohn's Disease?**
  - a. If yes, go to #7
  - b. If no, forward to clinical for review

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- 7) **Will the patient be on concurrent therapy with Anakinra, a TNF-inhibitor or an immunosuppressant other than corticosteroids (e.g. 6-mercaptopurine, azathioprine, cyclosporine, methotrexate)?**  
(Aminosalicylates may be continued during treatment with Tysabri)
- If yes, forward to clinical for review
  - If no and induction therapy, go to #8
  - If no and renewal for maintenance therapy, go to #9
- 8) **Did the patient have an inadequate response to, or is unable to tolerate conventional therapies for Chron's Disease, such as a TNF-inhibitor?**
- If yes, and induction - approve for 12 weeks
  - If no, forward to clinical for review
- 9) **Has the patient experienced therapeutic benefit after 12 weeks of induction therapy?**
- If yes, go to #10
  - If no, forward to clinical for review
- 10) **Is the patient being treated with oral corticosteroids?**  
Duration of corticosteroid therapy: \_\_\_\_\_
- If yes and the patient has been on Tysabri for less than 6 months, then approve for the remainder left of the 6 month period such that total use equals 6 months. (Note: If a patient cannot be tapered off oral corticosteroids within 6 months of initiating Tysabri, then treatment with Tysabri should be discontinued)
  - If yes and the patient has been on Tysabri for 6 months, forward to clinical for review. (Note: If a patient cannot be tapered off oral corticosteroids within 6 months of initiating Tysabri, then treatment with Tysabri should be discontinued)
  - If yes and patient has been on therapy more than 6 months, go to #11
  - If no, approve for 3 months
- 11) **Has the patient required oral corticosteroid use that exceeds 3 months in a calendar year?**
- If yes, forward to clinical for review
  - If no, approve for 3 months
- 12) **Approve for 6 months initiation with a quantity level limit of 1 x 300mg vial per 30 days**

**RENEWAL CRITERIA:**

- 1) **Has the patient demonstrated continued response to therapy?**
- If yes, go to #2
  - If no, forward to clinical
- 2) **Approve for 12 months maintenance with a quantity level limit of 1 x 300mg vial per 30 day**

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**Special Instructions:**

**Boxed Warnings:**

- *Tysabri increases the risk of progressive multifocal leukoencephalopathy (PML), a viral infection of the brain that usually leads to death or severe disability. Due to the risk of PML, Tysabri is available only through a special restricted distribution program called the TOUCH prescribing program. Only prescribers, infusion centers and pharmacies associated with the infusion centers registered with the program are able to prescribe, distribute or infuse Tysabri. Only patients who are enrolled in and meet all the conditions of the TOUCH prescribing program are able to receive the medication.*
- *Healthcare professionals should monitor patients on Tysabri for any new sign or symptom that may be suggestive of PML. For diagnosis, an evaluation that includes a gadolinium-enhanced MRI scan of the brain and, when indicated, cerebrospinal fluid analysis for JC viral DNA are recommended.*

**Warnings:**

- *Tysabri has been associated with hypersensitivity reactions, including serious systemic reactions (i.e. anaphylaxis) which occurred in <1% of people taking Tysabri. These reactions usually occur within 2 hours of the start of the infusion. Symptoms associated with these reactions can include urticaria, dizziness, fever, rash, rigors, pruritus, nausea, flushing, hypotension, dyspnea and chest pain.*
- *Immune system effects of Tysabri may increase the risk for infections such as pneumonias, urinary tract infections, gastroenteritis, vaginal infections, tooth infections, tonsillitis and herpes infection.*
- *Concurrent use of antineoplastic, immunosuppressant or immunomodulating agents may further increase the risk of infections, including PML and other opportunistic infections, over the risk observed with use of Tysabri alone.*
- *Concurrent use of short courses of corticosteroids was associated with an increase in infections.*

**Clinical Information:**

- *Pregnancy Category C*
- *If a woman becomes pregnant while taking Tysabri, consider enrolling her in the Tysabri Pregnancy Exposure Registry 1-800-456-2255.*
- *Persistently-positive antibodies (antibodies detected at  $\geq 2$  different time points which are  $\geq 42$  days apart) occur in about 6% of people taking Tysabri and are associated with substantial decrease in efficacy, decrease in serum Tysabri levels and increase in infusion and hypersensitivity reactions.*

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***Dosing:***

- *300 mg IV infusion every four weeks*
- *Recommended for use in > 18 years of age*

***Storage:***

- *Tysabri single-use vials must be refrigerated between 2-8 degrees C (36-46 degrees F). Protect from light. Do not shake or freeze.*