Tysabri (Natalizumab) Prior Approval Criteria
January 2016

OVERVIEW

Natalizumab (Tysabri®, Biogen Idec, Inc., Cambridge, MA), is a recombinant humanized IgG4κ monoclonal antibody produced in murine myeloma cells. The specific mechanism(s) by which natalizumab exerts its effects in multiple sclerosis (MS) and Crohn’s disease have not been fully defined. In relapsing forms of multiple sclerosis, the drug has been shown to reduce relapses and the appearance of new brain lesions. Natalizumab is also utilized for treatment of moderately to severely active Crohn’s disease.

Risk Evaluation and Mitigation Strategies (REMS)

Tysabri is available only through a restricted program under a REMS program called the TOUCH® Prescribing Program because of the risk of progressive multifocal leukoencephalopathy (PML). Some program requirements include that prescribers must be certified with the program by enrolling and completing training. Also, patients must enroll in the program and comply with ongoing monitoring requirements. Pharmacies and infusion centers must be specially certified to dispense or infuse. Patients need to be evaluated three months after the first infusion, six months after the first infusion, every six months thereafter, and for at least six months after discontinuing Tysabri. Prescriber must determine every six months whether patients should continue on treatment and, if so, authorize treatment for another six months. Status reports and discontinuation questionnaires must be completed.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Tysabri injection. Because of the specialized skills required for evaluation and diagnosis of patients treated with Tysabri as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Tysabri to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 1 year in duration unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tysabri (natalizumab) is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

A) Patient is currently receiving Tysabri. Approve for 1 year for patients who have had a history of beneficial response to this medication and Tysabri for an indication or condition addressed as an approval in the Recommended Authorization Criteria section (FDA-Approved Indications).

B) Initial Therapy

i. For all FDA Approved Indications: coverage is provided when this medication is NOT being used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, methotrexate) or TNF-alpha inhibitors (e.g., adalimumab, certolizumab pegol, infliximab); AND
ii. For Crohn’s Disease - induction of remission of moderate to severe, approve in patients who meet the following criteria (a, b, c, d, e and f). For Crohn’s Disease - maintenance of remission of moderate to severe, approve in patients who meet the following criteria (a, d, e and f).

a. The patient is ≥ 18 years of age; AND
b. Coverage is provided for patients who have experienced failure of, intolerance to or are unable to receive Aminosalicylates (e.g., sulfasalazine, mesalamine, balsalazide); AND
c. Coverage is provided for patients who have experienced failure of, intolerance to or are unable to receive Corticosteroids (e.g., prednisone); AND
d. Coverage is provided for patients who have experienced failure of, intolerance to or are unable to receive immunomodulators (e.g., azathioprine, 6-mercaptopurine, methotrexate); AND
e. Coverage is provided for patients who have experienced failure of a 2 month trial, intolerance to or are unable to receive AT LEAST 2 TNF-alpha inhibitors (e.g., adalimumab, certolizumab pegol, infliximab); AND
f. Tysabri is prescribed by or in consultation with a gastroenterologist. Approve for 6 months.

iii. For relapsing remitting multiple sclerosis (RRMS), approve in patients who meet the following criteria (a, b and c).

a. The patient is ≥ 18 years of age; AND
b. Coverage is provided for patients who have experienced failure of a trial of AT LEAST 1 month per drug, intolerance to or are unable to receive at least one therapeutic agent from two or more of the following drug categories: Interferon beta-1a or interferon beta-1b (for example, Avonex, Rebif, Betaseron, Extavia ), Glatiramer acetate (Copaxone), Fingolimod (Gilenya), OR Teriflunomide (Aubagio); AND
c. Tysabri is prescribed by or in consultation with a neurologist or a physician that specializes in the treatment of MS. Approve for 6 months.

**Dosing**

300 mg intravenous infusion every 4 weeks

**Approval Duration**

Initial Approval = 6 months (180 days)
Re-authorization = 1 year (365 days)

**CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Tysabri has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Children with Multiple Sclerosis (MS) or Crohn’s Disease.** Tysabri is not indicated in pediatric patients with MS or Crohn’s disease who are < 18 years of age. There have been case series reports of use of Tysabri in adolescents aged 12 to 17 years with RRMS who were refractory to other...
agents. Long-term risks of using Tysabri in children are not known. Interferon beta and Copaxone are the two most frequently used disease modifying therapies used in pediatric patients with RRMS in the US. Limited information is available on use of Tysabri in adolescents with Crohn’s disease.

2. **Concurrent Use of Tysabri with an Immunosuppressant Agent in Patients with Crohn’s Disease.** Tysabri should not be given in combination with an immunosuppressant agent (6-mercaptopurine, azathioprine, cyclosporine, or MTX or with a TNFα inhibitor [e.g., Remicade, Humira, Cimzia]). Tysabri is not indicated in combination with these agents. Aminosalicylates may be continued during therapy with Tysabri. Tysabri can be started in patients on chronic oral corticosteroids, but patients should be tapered off corticosteroids.

3. **Current Use of Tysabri with Other Disease-Modifying Agents Used for Multiple Sclerosis (MS) or with an Immunosuppressant in Patients with MS.** Tysabri should not be given in combination with other disease-modifying agents used for MS (e.g., Betaseron/Extavia, Rebif, Copaxone/Glatopa, Avonex, Lemtrada, Plegridy, Gilenya, Aubagio, Tecfidera) or with an immunosuppressant such as mitoxantrone, cyclophosphamide, Rituxan® (rituximab injection for IV infusion), Campath® (alemtuzumab injection for IV infusion), azathioprine, MTX, or mycophenolate mofetil. Tysabri is only indicated as monotherapy due to an increased risk of PML. Ordinarily, patients with MS who are receiving chronic immunosuppressant or immunomodulatory therapy should not take Tysabri.

4. **Immune Compromised Patients with Multiple Sclerosis (MS) or Crohn’s Disease.** Patients with a medical condition that results in significantly compromised immune system function such as human immunodeficiency virus (HIV) infection, leukemia, lymphoma, or organ transplant should not ordinarily be treated with Tysabri.

5. **Primary Progressive (Chronic Progressive) Multiple Sclerosis (MS).** The safety and efficacy of Tysabri have not been studied in patients with primary progressive (chronic progressive) MS. Tysabri is indicated in patients with relapsing forms of MS.

6. **Ulcerative Colitis.** Efficacy data with use of Tysabri are limited.

7. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

- Tysabri injection [prescribing information]. South San Francisco, CA: Elan Pharmaceuticals, Inc.; (manufactured by Biogen Idec Inc); May 2015.


Copaxone® [prescribing information]. Kansas City, MO: Teva Neuroscience; October 2014.
Aubagio® [prescribing information]. Cambridge, MA: Genzyme (a Sanofi Corporation); October 2014a.
Gilenya® [prescribing information]. East Hanover, NJ: Novartis; August 2015.
Tecfidera® [prescribing information]. Cambridge, MA: Biogen Idec; April 2015.


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