Tysabri (Natalizumab) Prior Approval
August 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. All approvals are provided for 1 year in duration unless otherwise noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Automation: None.

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

Food and Drug Administration (FDA)-Approved Indications

1. Relapsing Form of Multiple Sclerosis (MS) in an Adult.

Criteria. Approve in patients who meet the following criteria (A, B, C, D, and E):
A) The patient is ≥ 18 years of age; AND
B) The patient has a relapsing form of MS (relapsing forms of MS are Relapsing-remitting MS, Secondary-progressive MS with relapses, and Progressive-relapsing MS); AND
C) Failure of (trial of ≥1 month per drug), intolerance to or unable to receive (e.g., interferon not recommended in an individual with depression/mood disorder) at least one therapeutic agent from **two or more** of the following drug categories:
   1. Interferon beta-1a (e.g., Avonex®, Plerady®, Rebif®) or interferon beta-1b (e.g., Betaseron®, Extavia®); or
   2. Glatiramer acetate (Copaxone®, Glatopa®); or
   3. Fingolimod (Gilenya®); or
   4. Teriflunomide (Aubagio®); or
   5. Dimethyl fumarate (Tecfidera®); or
   6. Alemtuzumab (Lemtrada®); or
   7. Daclizumab (Zinbryta®).

D) Natalizumab will not be used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, methotrexate) or other disease-modifying agents (e.g., interferon beta-1a, interferon beta-1b, glatiramer acetate); AND

E) Tysabri is prescribed by, or in consultation with, a physician who specializes in the treatment of multiple sclerosis (MS) and/or a neurologist.

**Dosing:** 300 mg intravenous infusion every 4 weeks

**Approval Duration**
Initial Approval = 6 months.
Re-authorization = 1 year

2. **Crohn’s Disease in an Adult.**

**Criteria.**

*For Crohn’s Disease- induction of remission of moderate to severe, Approve in patients who meet the following criteria (A, B, C, D, E, F, and G).*

*For Crohn’s Disease - maintenance of remission of moderate to severe, Approve in patients who meet the following criteria (A, D, E, F, and G).*

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-α inhibitors (e.g., adalimumab, certolizumab pegol, infliximab); AND

F) Natalizumab will not be used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, methotrexate) or TNF-α inhibitors (e.g., adalimumab [Humira], certolizumab pegol [Cimzia], infliximab [Remicade]); AND

G) Tysabri is prescribed by or in consultation with a gastroenterologist.
Dosing: 300 mg intravenous infusion every 4 weeks

**Approval Duration**
Initial Approval = 3 months
Re-authorization = 1 year

3. **Patient has been Started on Tysabri.**

*For Relapsing Form of Multiple Sclerosis (MS) in an Adult-* The patient must meet the following criteria (A, B, C, D, E and F):

A) The patient has a history of beneficial response to Natalizumab; AND
B) The patient is ≥ 18 years of age; AND
C) The patient has a relapsing form of MS (relapsing forms of MS are Relapsing-remitting MS, Secondary-progressive MS with relapses, and Progressive-relapsing MS); AND
D) Natalizumab will not be used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, methotrexate) or other disease-modifying agents (e.g., interferon beta-1a, interferon beta-1b, glatiramer acetate); AND
E) Tysabri is prescribed by, or in consultation with, a physician who specializes in the treatment of multiple sclerosis (MS) and/or a neurologist; AND
F) Dosage and administration are consistent with U.S. Food and Drug Administration approved label (i.e., 300 mg intravenous infusion every four weeks.)

*For Crohn’s Disease-* The patient must meet the following criteria (A, B, C, D, and E).

A) The patient has a history of beneficial response to Natalizumab; AND
B) The patient is ≥ 18 years of age; AND
C) Natalizumab will not be used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, methotrexate) or TNF-α inhibitors (e.g., adalimumab [Humira], certolizumab pegol[Cimzia], infliximab[Remicade]); AND
D) Tysabri is prescribed by or in consultation with a gastroenterologist; AND
E) Dosage and administration are consistent with U.S. Food and Drug Administration approved label (i.e., 300 mg intravenous infusion every four weeks).

**Approval Duration:** Approve for 1 year.

**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.


