Geisinger

POLICIES AND PROCEDURE MANUAL

Policy: MBP 57.0

Section: Medical Benefit Pharmaceutical Policy

Subject: Tysabri (natalizumab)

I. Policy:
Tysabri (natalizumab)

II. Purpose/Objective:
To provide a policy of coverage regarding Tysabri (natalizumab)

III. Responsibility:
A. Medical Directors
B. Medical Management
C. Pharmacy Department

IV. Required Definitions
1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than
3. the department requiring/authoring the policy.
4. Devised – the date the policy was implemented.
5. Revised – the date of every revision to the policy, including typographical and grammatical changes.
6. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient

Medicaid Business Segment
Medically Necessary — A service, item, procedure, or level of care compensable under the Medical Assistance program that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

i. Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
ii. Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
iii. Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.

DESCRIPTION:
Tysabri (natalizumab) is a monoclonal antibody bioengineered from part of a mouse antibody to closely resemble a human antibody and binds to a protein called alpha-4-integrin. Integrins are found primarily on the surface of white blood cells which are thought to play a major role in causing the damage to the nervous system in multiple sclerosis (MS). Natalizumab blocks adhesion and subsequent migration of leukocytes into the gut by binding the α - 4 integrin thereby reducing chronic inflammation associated with Crohn's disease.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee

GRANDFATHER PROVISION – Members already established on therapy are eligible for approval as long as there is medical record documentation that the safety and effectiveness of use for the prescribed indication is supported by Food and Drug Administration (FDA) approval or adequate medical and scientific evidence in the medical literature

Tysabri (natalizumab) will be considered medically necessary for commercial, exchange, and CHIP lines of business when all of the following criteria are met:

1. **Relapsing Multiple Sclerosis**
   Tysabri is considered medically necessary for the treatment of relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease when the following criteria are met:

   - Medical record documentation of member being established on and responding to Tysabri

   OR

   - Medical record documentation of a diagnosis of a relapsing form of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease **AND**
   - Medical record documentation that the patient 18 years or older **AND**
   - Medical record documentation that Tysabri is being prescribed by a neurologist **AND**
   - Physician documentation that Tysabri is being used as monotherapy is provided **AND**
   - Medical record documentation that the member has been tested for anti-JCV antibody prior to start of Tysabri therapy
     - If patient is anti-JCV antibody positive, medical record documentation that benefits of drug outweigh the risks of progressive multifocal leukoencephalopathy (PML) and patient is aware of increased PML risk

   AND
   - Medical record documentation of therapeutic failure on, contraindication to, or intolerance to two formulary alternatives OR medical record documentation of highly active disease course requiring aggressive treatment

   NOTE: According to the American Academy of Neurology recommendation, Tysabri may be considered as a first line therapy in individuals with relapsing remitting multiple sclerosis who exhibit particularly aggressive initial course of disease and in whom the potential benefit is felt to outweigh the risk. Patients with a poor prognosis/aggressive disease include those with a heavy T2 lesion load, lesions in brain stem, cerebellum, and spinal cord.

   LIMITATIONS:
   - Cannot be used in combination with immunosuppressants (i.e. 6-mercaptopurine, azathioprine, cyclosporine, methotrexate) or inhibitors of TNF-alpha

   AUTHORIZATION DURATION:
   Initial authorization and reauthorizations for MS will be for a period of one (1) year. For re-authorization, medical record documentation of patient adherence to medication and improvement or stabilization of the multiple sclerosis disease course while on Tysabri therapy will be required.
   - For patients who were previously anti-JCV antibody negative, medical record documentation that physician has re-tested for anti-JCV antibody status within the last 12 months.
   - For patients who were anti-JCV antibody positive at baseline or on re-test, medical record documentation that benefits of continuing drug outweigh risks.

2. **Crohn's disease**
Tysabri® is considered medically necessary as a second line therapy after conventional therapy and TNF inhibitors, when the following criteria are met:

The insured individual

- Must be 18 years of age or older **AND**
- Has had a formal consultation with a gastroenterologist and recommendation for treatment with natalizumab **AND**
- Has a diagnosis of active Crohn's disease considered to be moderate or severe based on clinical signs and symptoms and documented contraindication to, intolerance to, or failure on adequate conventional therapy; (corticosteroids, 5-aminosalicylates, and/or 6-mercaptopurine/azathioprine, methotrexate) and an inadequate response to, contraindication to, or failure on 12 weeks of adalimumab (Humira) therapy and 12 weeks of infliximab (Remicade) therapy **AND**
- Is enrolled in a risk-minimization program, called the TOUCH™ Prescribing Program

AUTHORIZATION DURATION:
Initial approval for treatment of Crohn's disease will be for 12 weeks. For continuation of coverage, the following information is required for submission by the prescribing provider:

- Documentation of therapeutic benefit **AND**
- Documentation that concomitant steroids will be discontinued within 6 months of starting therapy.

Subsequent approvals will be for a 6 month time frame.

CONTRAINDICATIONS:
Natalizumab is contraindicated in patients who have or have had progressive multifocal leukoencephalopathy (PML) or with known hypersensitivity to natalizumab or any of its components.

LIMITATIONS:
Tysabri is FDA-approved for use only as a stand-alone treatment that cannot be administered in conjunction with additional MS treatments. Combining other therapies with natalizumab is thought to increase the risk of PML.

Tysabri (natalizumab) will be considered medically necessary for the Medicare line of business when all of the following criteria are met:

1. **Relapsing Multiple Sclerosis**
Tysabri is considered medically necessary for the treatment of relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease when the following criteria are met:

- Medical record documentation of member being established on and responding to Tysabri

OR

- Medical record documentation of a diagnosis of a relapsing form of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease **AND**
- Medical record documentation that the patient 18 years or older **AND**
- Medical record documentation that Tysabri is being prescribed by a neurologist **AND**
- Physician documentation that Tysabri is being used as monotherapy is provided **AND**
- Medical record documentation that the member has been tested for anti-JCV antibody prior to start of Tysabri therapy
    - If patient is anti-JCV antibody positive, medical record documentation that benefits of drug outweigh the risks of progressive multifocal leukoencephalopathy (PML) and patient is aware of increased PML risk

AND

- Medical record documentation of therapeutic failure on, contraindication to, or intolerance to two formulary alternatives OR medical record documentation of highly active disease course requiring aggressive treatment

NOTE: According to the American Academy of Neurology recommendation, Tysabri may be considered as a first line therapy in individuals with relapsing remitting multiple sclerosis who exhibit particularly aggressive initial course of disease and in whom the potential benefit is felt to outweigh the risk. Patients with a poor prognosis/aggressive disease include those with a heavy T2 lesion load, lesions in brain stem, cerebellum, and spinal cord.

LIMITATIONS:

- Cannot be used in combination with immunosuppressants (i.e. 6-mercaptopurine, azathioprine, cyclosporine, methotrexate) or inhibitors of TNF-alpha

AUTHORIZATION DURATION:
Initial authorization and reauthorizations for MS will be for a period of one (1) year. For re-authorization, medical record documentation of patient adherence to medication and improvement or stabilization of the multiple sclerosis disease course while on Tysabri therapy will be required.

- For patients who were previously anti-JCV antibody negative, medical record documentation that physician has re-tested for anti-JCV antibody status within the last 12 months.
- For patients who were anti-JCV antibody positive at baseline or on re-test, medical record documentation that benefits of continuing drug outweigh risks.

2. Crohn's disease
Tysabri® is considered medically necessary as a second line therapy after conventional therapy and TNF inhibitors, when the following criteria are met:

The insured individual

- Must be 18 years of age or older **AND**
- Has had a formal consultation with a gastroenterologist and recommendation for treatment with natalizumab **AND**
- Has a diagnosis of active Crohn's disease considered to be moderate or severe based on clinical signs and symptoms and documented contraindication to, intolerance to, or failure on adequate conventional therapy; (corticosteroids, 5-aminosalicylates, and/or 6-mercaptopurine/azathioprine, methotrexate) and an inadequate response to, contraindication to, or failure on 12 weeks of adalimumab (Humira) therapy and 12 weeks of infliximab (Remicade) therapy **AND**
- is enrolled in a risk-minimization program, called the TOUCH™ Prescribing Program

AUTHORIZATION DURATION:
Initial approval for treatment of Crohn's disease will be for 12 weeks. For continuation of coverage, the following information is required for submission by the prescribing provider:

- Documentation of therapeutic benefit **AND**
- Documentation that concomitant steroids will be discontinued within 6 months of starting therapy.

Subsequent approvals will be for a 6 month time frame.

CONTRAINDICATIONS:
Natalizumab is contraindicated in patients who have or have had progressive multifocal leukoencephalopathy (PML) or with known hypersensitivity to natalizumab or any of its components.

LIMITATIONS:
Tysabri is FDA-approval for use only as a stand-alone treatment that cannot be administered in conjunction with additional MS treatments. Combining other therapies with natalizumab is thought to increase the risk of PML.

LINE OF BUSINESS:
Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy.

REFERENCES:

1. Tysabri [prescribing information]. Cambridge, MA: Biogen Inc; October 2023.
2. Rae-Grant A, Day GS, Marie RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis. American Academy of Neurology (AAN). Neurology; 2018 Apr 23; 90(17):777-788 [cited 2023 Dec 27]. Available from: https://www.neurology.org/doi/pdf/10.1212/WNL.0000000000005347

This policy will be revised as necessary and reviewed no less than annually**.**

Devised: 8/2/06

Revised: 5/08 (added indication), 8/10 (clarified indication); 10/11 (clarified indication); 2/12 (clarify indications), 11/18/14 (updated criteria for MS and added auth duration), 9/20/16 (MS criteria changes), 9/8/17(updated dx language), 7/10/19 (grandfather), 9/17/19 (MS definition), 7/19/22 (MS edits, LOB carve out), 7/12/23 (Medicaid business segment), 12/31/23 (references added)

Reviewed: 8/09, 8/11; 4/14; 11/18/2014, 11/2/2015, 7/31/17, 7/10/18, 5/31/19, 9/10/20, 8/27/21, 6/28/24

MA UM Committee approval: 12/31/23