Tysabri

Description

Tysabri (natalizumab)

Background
Tysabri is used to prevent episodes of symptoms and slow the worsening of disability in patients with relapsing forms (course of disease where symptoms flare up from time to time) of multiple sclerosis (MS). Tysabri is also used to treat and prevent episodes of symptoms in people who have Crohn's disease (a condition in which the body attacks the lining of the digestive tract, causing pain, diarrhea, weight loss, and fever) who have not been helped by other medications or who cannot take other medications. Tysabri is in a class of medications called immunomodulators. It works by stopping certain cells of the immune system from reaching the brain and spinal cord and causing damage (1).

Regulatory Status
FDA-approved indication: Tysabri is an integrin receptor antagonist indicated for treatment of (1):

Multiple Sclerosis (MS) - As monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. Tysabri increases the risk of PML. Tysabri is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate MS therapy. When initiation or continuing treatment with Tysabri, physicians should consider whether the expected benefit of Tysabri is sufficient to offset the risks.

Crohn's Disease (CD) - Inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who
have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-α.

Limitations of Use: (1)
In Crohn’s disease, Tysabri should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α.

Tysabri carries a boxed warning regarding the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. Tysabri is contraindicated in patients who have or have had progressive multifocal leukoencephalopathy (PML). Monitor patients and withhold Tysabri at the first sign or symptom suggestive of PML. Duration of Tysabri exposure, prior immunosuppressant use, and presence of anti-JC virus antibodies are associated with increased risk of PML in Tysabri-treated patients. There is limited experience in patients who have received more than 4 years of Tysabri treatment (1).

The immune system effects of Tysabri may increase the risk for infections. 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 the use of Tysabri alone. Patients should be monitored for development of infections due to increased risk with use of Tysabri (1).

The safety and efficacy of Tysabri in combination with antineoplastic, immunosuppressant, or immunomodulating agents have not been established. Patients receiving chronic immunosuppressant or immunomodulatory therapy or who have systemic medical conditions resulting in significantly compromised immune system function should not ordinarily be treated with Tysabri. The risk of PML is also increased in patients who have been treated with an immunosuppressant prior to receiving Tysabri (1).

For patients with Crohn’s disease who start Tysabri while on chronic corticosteroids, commence steroid withdrawal as soon as a therapeutic benefit has occurred. If the patient cannot discontinue systemic corticosteroids within six months, discontinue Tysabri (1).

Clinically significant liver injury has occurred. Signs of liver injury, including markedly elevated serum hepatic enzymes and elevated total bilirubin, occurred as early as six days after the first dose; signs of liver injury have also been reported for the first time after multiple doses. Tysabri should be discontinued in patients with jaundice or evidence of liver injury (1).
Because of the risk of PML, Tysabri is available only under a restricted distribution program, the TOUCH Prescribing Program (1).

Live, attenuated vaccines are generally not recommended for a person with MS because their ability to cause disease has been weakened but not totally inactivated (2).

Safety and effectiveness of Tysabri in pediatric patients with multiple sclerosis or Crohn’s disease below the age of 18 years have not been established. Tysabri is not indicated for use in pediatric patients (1).

**Related policies**
Acthar Gel, Ampyra, Aubagio, Gilenya, MS Injectables, Tecfidera

**Policy**
*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Tysabri may be considered *medically necessary* in patients 18 years of age and older as a monotherapy treatment in the relapsing form of Multiple Sclerosis for patients who have had an inadequate response, intolerance, or contraindication to an alternate MS therapy; not given concurrently with live vaccines and who are enrolled with the Risk Evaluation and Mitigation Strategy (REMS) called the TOUCH Prescribing Program. Tysabri may be considered *medically necessary* to induce or maintain a clinical response and remission in adult patients with moderately to severely active Crohn’s disease (CD) with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-α; enrolled with the Risk Evaluation and Mitigation Strategy (REMS) called the TOUCH Prescribing Program.

Tysabri is considered *investigational* in patients that are less than 18 years of age and for all other indications.

**Prior-Approval Requirements**

**Age**
18 years of age or older

**Diagnoses**

Patient must have ONE of the following:
1. Relapsing form of Multiple Sclerosis
   a. Used as monotherapy
   b. Inadequate response, intolerance, or contraindication to another MS therapy

2. Crohn’s Disease
   a. Moderately to severely active
   b. Inadequate response, intolerance, or contraindication to ALL of the following:
      i. Conventional Crohn’s disease therapies
      ii. TNF inhibitors
   c. NOT to be used in combination with immunosuppressants or TNF inhibitors.

AND ALL of the following:
   a. Patient does NOT have or have had progressive multifocal leukoencephalopathy (PML)
   b. Patient will be monitored for any new sign or symptom that may be suggestive of PML
      i. Tysabri will be withheld at the 1st sign or symptom suggestions of PML.
   c. Patient does NOT have significantly compromised immune system function.
   d. Patient must be enrolled in and meet all conditions of the TOUCH Prescribing Program
   e. NOT given concurrently with live vaccines

Prior – Approval Renewal Requirements

Age 18 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Relapsing form of Multiple sclerosis
   a. Used as monotherapy
2. Crohn's Disease
   a. **NOT** to be used in combination with immunosuppressants or inhibitors of TNF-α.
   b. Patient has experienced therapeutic benefit by 12 weeks of induction therapy.

   **AND ALL** of the following:
   a. Patient does not have progressive multifocal leukoencephalopathy (PML)
   b. Patient must be enrolled in and meet all conditions of the TOUCH Prescribing Program
   c. **NO** concurrent therapy with systemic corticosteroids
   d. **NO** evidence of jaundice or liver injury
   e. **NO** development of opportunistic infections
   f. **NOT** given concurrently with live vaccines

---

**Policy Guidelines**

**Pre - PA Allowance**
None

**Prior - Approval Limits**

Duration  4 months

**Prior – Approval Renewal Limits**

Duration  12 months

---

**Rationale**

**Summary**

Tysabri is used to prevent episodes of symptoms and slow the worsening of disability in patients with relapsing forms of multiple sclerosis. Tysabri is also used to treat and prevent episodes of symptoms in people who have Crohn's disease who have not been helped by other medications or who cannot take other medications. In CD, Tysabri should not be used in combination with immunosuppressants or inhibitors of TNF-α. Tysabri carries a boxed warning regarding the risk of progressive multifocal leukoencephalopathy (PML). The immune system effects of Tysabri may increase the risk for infections. The safety and efficacy of Tysabri in combination with antineoplastic, immunosuppressant, or immunomodulating agents have not been established.
Tysabri is not indicated for use in pediatric patients. Tysabri should be discontinued in patients with jaundice or evidence of liver injury. Because of the risk of PML, Tysabri is available only under a special restricted distribution program, the TOUCH prescribing program (2). Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Tysabri while maintaining optimal therapeutic outcomes.

References

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 2013</td>
<td>Addition to PA</td>
</tr>
<tr>
<td>September 2014</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td></td>
<td>Removal of evidence of inflammation</td>
</tr>
<tr>
<td>December 2014</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>March 2015</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>September 2016</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td></td>
<td>Policy number changed from 5.08.27 to 5.60.13</td>
</tr>
<tr>
<td>December 2016</td>
<td>Addition of age limits to renewal criteria</td>
</tr>
<tr>
<td></td>
<td>Change in duration of prior approval limits for initiation from 6 months to 4 months</td>
</tr>
<tr>
<td></td>
<td>Addition of not given concurrently with live vaccines to MS indication</td>
</tr>
<tr>
<td>March 2017</td>
<td>Annual review</td>
</tr>
<tr>
<td>June 2017</td>
<td>Annual review</td>
</tr>
</tbody>
</table>

Keywords

This policy was approved by the FEP Pharmacy and Medical Policy Committee on June 22, 2017 and is effective on July 1, 2017.