MDWISE PRIOR AUTHORIZATION CRITERIA
TYSABRI® (natalizumab): 300mg/15mL single use vial

Formulary Status: Non-Formulary requiring prior authorization

PA CRITERIA FOR INITIAL AUTHORIZATION FOR USE IN MULTIPLE SCLEROSIS (MS):

- Documentation submitted indicates that the member is an adult (≥ 18 y/o) and has a clinical diagnosis of a relapsing form of multiple sclerosis.
- Clinical and/or diagnostic information was submitted that indicates that the patient has a documented (consistent with pharmacy claims data OR for new members to the health plan consistent with medical chart history) treatment failure (see Box 1 for definition of treatment failure) after receiving an adequate trial (including dates, doses of 6 months or more of each therapy) of interferon Beta-1A (Rebif®) and glatiramer acetate (Copaxone®) and/or has a some other documented medical reason (intolerance, hypersensitivity, etc) for not utilizing all of these therapies for a minimum of 6 months each to manage their medical condition.
- Documentation consistent with pharmacy claims data was submitted indicating the patient is not currently using any antineoplastic, immunosuppressant, or immunomodulating medications and does not have a history of progressive multifocal leukoencephalopathy (PML) and does not have a compromised immune system.
- TYSABRI is being prescribed at an FDA approved dosage.

If all of the above conditions are met, the request will be approved for up to a 6-month duration; if all of the above criteria are not met the request will be referred to a Medical Director for medical necessity review.

PA CRITERIA FOR REAUTHORIZATION FOR USE IN MS:

- Documentation was submitted indicating that the member is an adult (≥ 18 y/o) and has a current clinical diagnosis of a relapsing form of multiple sclerosis.
- Diagnostic and/or clinical documentation was submitted (e.g. improved disease activity index, quality of life, blood work, radiographic evidence etc.) that indicates the member has significantly clinically benefited from receiving TYSABRI therapy.
- Documentation consistent with pharmacy claims data was submitted indicating the patient is not currently using any antineoplastic, immunosuppressant, or immunomodulating medications and does not have a history of progressive multifocal leukoencephalopathy (PML) and does not have a compromised immune system.
- TYSABRI is being prescribed at an FDA approved dosage.

If all of the above conditions are met, the request will be approved for up to a 6-month duration; if all of the above criteria are not met the request will be referred to a Medical Director for medical necessity review.

PA CRITERIA FOR INITIAL APPROVAL FOR CROHN’S DISEASE:

- The member is an adult (≥ 18 y/o) and has a documented clinical diagnosis of moderate to severely active Crohn’s Disease
- The patient has a documented (consistent with pharmacy claims data, OR for new members to the health plan consistent with medical chart history) adequate trial (including dates and doses) at therapeutic doses and/or has some documented clinically significant medical reason (intolerance, hypersensitivity, etc) for not receiving oral conventional therapy to manage their medical condition.
- The patient has a documented (consistent with pharmacy claims data, OR for new members to the health plan consistent with medical chart history) adequate trial (including dates and doses) with therapeutic doses of and/or has some documented clinically significant medical reason for not receiving Humira® (adalimumab).
- TYSABRI is being prescribed by a gastroenterologist at an FDA approved dosage.

If all of the above conditions are met, the request will be approved for up to a 6-month duration; if all of the above criteria are not met the request will be referred to a Medical Director for medical necessity review.

PA CRITERIA FOR REAUTHORIZATION FOR USE IN CROHN’S DISEASE:

- Documentation was submitted indicating that the member is an adult (≥ 18 y/o) and has a documented clinical diagnosis of moderate to severely active Crohn’s Disease
Diagnostic and/or clinical documentation was submitted (e.g. improved disease activity index, quality of life, blood work, radiographic evidence etc.) that indicates the member has significantly clinically benefited from receiving TYSABRI therapy.

Documentation consistent with pharmacy claims data was submitted indicating the patient is not currently using any antineoplastic, immunosuppressant, or immunomodulating medications and does not have a history of progressive multifocal leukoencephalopathy (PML) and does not have a compromised immune system.

TYSABRI is being prescribed by a gastroenterologist at an FDA approved dosage.

If all of the above conditions are met, the request will be approved for up to a 6-month duration; if all of the above criteria are not met the request will be referred to a Medical Director for medical necessity review.

PA CRITERIA FOR INITIAL AUTHORIZATION FOR USE IN OTHER MEDICALLY ACCEPTED INDICATIONS:

- The medication is recommended and prescribed a specialist in the field to treat the member’s respective medical condition.
- The medication is prescribed for a medically accepted use per the medical compendia (i.e. Micromedex, DrugPoints, AHFS drug information) as defined by the Social Security Act.
- Documentation was submitted indicating that the member has a documented (consistent with pharmacy claims data) adequate trial (including dates, doses of medications) of all first line medical therapies as recommended by the medical compendia and standard of care guidelines and/or has a documented medical reason (i.e. intolerance, contraindications, etc.) for not receiving or trying all first line medical treatment(s).
- Documentation consistent with pharmacy claims data was submitted indicating the patient is not currently using any antineoplastic, immunosuppressant, or immunomodulating medications and does not have a history of progressive multifocal leukoencephalopathy (PML) and does not have a compromised immune system.
- Documentation on request form indicates that the medication is recommended or prescribed by a physician who is authorized by the TOUCH™ program to prescribe TYSABRI and that the patient is enrolled in the TOUCH™ program and has agreed to comply with the requirements for receiving TYSABRI.
- The medication is prescribed at a medically accepted dose per the medical compendia (i.e. Micromedex, DrugPoints, AHFS drug information) as defined by the Social Security Act.

If all of the above conditions are met, the request will be approved for up to a 6-month duration; if all of the above criteria are not met the request will be referred to a Medical Director for medical necessity review.

PA CRITERIA FOR RE-AUTHORIZATION FOR USE IN OTHER MEDICALLY ACCEPTED INDICATIONS:

- The medication is recommended or prescribed by a specialist for the respective treated disease state.
- Diagnostic and/or clinical documentation was submitted (e.g. improved disease activity index, quality of life, blood work, radiographic evidence etc.) that indicates the member has significantly clinically benefited from receiving TYSABRI therapy.
- Documentation on request form indicates that the medication is recommended or prescribed by a physician who is authorized by the TOUCH™ program to prescribe TYSABRI and that the patient is enrolled in the TOUCH™ program and has agreed to comply with the requirements for receiving TYSABRI.
- Documentation consistent with pharmacy claims data was submitted indicating the patient is not currently using any antineoplastic, immunosuppressant, or immunomodulating medications and does not have a history of progressive multifocal leukoencephalopathy (PML) and does not have a compromised immune system.
- Documentation that, and is being prescribed at a medically accepted dose per the medical compendia (i.e. micromedex, DrugPoints, AHFS) as defined by the Social Security Act.

If all of the above conditions are met, the request will be approved for up to a 3-month duration; if all of the above criteria are not met the request will be referred to a Medical Director for medical necessity review.

FDA INDICATIONS:

Multiple Sclerosis:
Tysabri is indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis in order to delay the accumulation of physical disability and to reduce frequency of clinical exacerbations. Tysabri is generally recommended for patients who have an inadequate response to, or are unable to tolerate, alternate multiple sclerosis therapies.

**Crohn’s Disease:**

Tysabri is indicated for 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 Crohn’s disease therapies and inhibitors to TNF-α.

**DOSAGE AND ADMINISTRATION:**

300 mg IV infused over approximately 1 hour, given at 4-week (28-day) intervals. Do not give as an intravenous push or bolus.

**BLACKBOX WARNING:**

TYSABRI (natalizumab) increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. Cases of PML have been reported in patients taking Tysabri who were recently or concomitantly treated with immunomodulators or immunosuppressants, as well as in patients receiving Tysabri as monotherapy.

**BOX 1: TREATMENT FAILURE:**

<table>
<thead>
<tr>
<th>A member may be considered to have failed treatment if any of the following are documented:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Member who has an attack rate (relapse) of more than 1 per year, fails to show a reduction in relapse rate, or continues to experience attacks (relapses) at a rate similar to that found before starting therapy**</td>
</tr>
<tr>
<td>2. Member who has incomplete recovery (cumulative residual abnormalities sustained for 6 months) from repeated attacks, particularly as the EDSS score increases. **</td>
</tr>
<tr>
<td>3. Member experiences an annual increase in the EDSS (Expanded Disability Status Scale) of 1 point from a previous score of 3 to 5.5, or 0.5 point increase from a previous score of 6.0 or greater in the absence of clinical attacks or other documentation of clinically significant disability progression. **</td>
</tr>
<tr>
<td>4. Member who develops new or recurrent brainstem or spinal cord lesions as seen on MRI. **</td>
</tr>
<tr>
<td>5. Members experiencing relapses affecting multiple neurologic symptoms, and those accumulating residual impairments in multiple neurologic systems. **</td>
</tr>
<tr>
<td>6. Members who have progressive motor, cognitive or sensory impairment sufficient to disrupt their daily activities irrespective of changes on neurologic examination, provided the influence of depression, medications or superimposed concurrent disease is ruled out. Examples include: loss of endurance in sustaining activity, forced alterations in activities of daily living, muddled thinking, impaired concentration and mental processing and fatigue. **</td>
</tr>
<tr>
<td>7. Members who have new or enlarging T2 lesions, brain atrophy on MRI, or new T1 Gd enhancing lesions on MRI accompanied by changes in the ability to perform daily activities. **</td>
</tr>
</tbody>
</table>

**These are members who have a documented treatment failure after receiving a minimum of 6 months each of Copaxone and Rebif. Diagnostic and/or clinical documentation of treatment failure will be required for the last therapy the member received. This requires that he member has failed a minimum of 6 months of all 3 available therapies (Rebif and Copaxone) and/or has a documented medical reason (i.e. intolerance) for not utilizing all 3 therapies for a minimum of 6 months.

**GLOSSARY:**

**TOUCH™:** is a distribution program designed to assess the risk of progressive multifocal leukoencephalopathy (PML) associated with TYSABRI, minimize the risk of PML, minimize the death and disability due to PML, and promote informed risk-benefit decisions regarding TYSABRI use.

**Kurtzke Expanded Disability Scale (EDSS) score:** is a scale for evaluating the degree of neurologic impairment in MS. The EDSS score is measured in one-half point increments, from 0.0 (*normal*) to 10.0 (*death*). In order to rate a person on the EDSS, the neurologist first performs a standard neurologic examination to test strength, coordination, vision, walking, etc. The neurologist next summarizes the results of the neurological examination in several “Functional
System Scores” as follows: pyramidal (strength and spasticity), cerebellar, brain stem, sensory, bowel and bladder, visual, cerebral and “other” functions. Finally, the neurologist uses the Functional System Scores along with ability to walk to rate the individual on the EDSS. The EDSS score is most reflective of lower limb function. Since this scoring system does not account for other signs and symptoms of MS, it is not used as an absolute measure of disability. But the EDSS can be a good gauge of disease progression. Other scales are used to measure fatigue, symptoms affecting the upper body, and mental changes.

Kurtzke Expanded Disability Status Scale (EDSS)

<table>
<thead>
<tr>
<th>Rating</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal Neurological Exam</td>
</tr>
<tr>
<td>1.0</td>
<td>No Disability, minimal symptoms</td>
</tr>
<tr>
<td>1.5</td>
<td>No disability, minimal signs in more than one area</td>
</tr>
<tr>
<td>2.0</td>
<td>Slightly more disability in one area</td>
</tr>
<tr>
<td>2.5</td>
<td>Slightly greater disability in two areas</td>
</tr>
<tr>
<td>3.0</td>
<td>Moderate disability in one area but still walking independently</td>
</tr>
<tr>
<td>3.5</td>
<td>Walking independently but with moderate disability in one area and more than minimal disability in several others</td>
</tr>
<tr>
<td>4.0</td>
<td>Walking without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability; able to walk without aid or rest some 500 meters</td>
</tr>
<tr>
<td>4.5</td>
<td>Walking without aid, up and about much of the day, able to work a full day, may have some limitation of full activity or require some help, relatively severe disability but able to walk without aid or rest some 300 meters.</td>
</tr>
<tr>
<td>5.0</td>
<td>Walking without aid or rest for about 200 meters, disability severe enough to impair full daily activities, can work a full day without special provisions</td>
</tr>
<tr>
<td>5.5</td>
<td>Ambulatory without aid or rest for about 100 meters; disability severe enough to prevent full daily activities</td>
</tr>
<tr>
<td>6.0</td>
<td>Intermittent or unilateral constant assistance (cane, crutch, brace) required to walk about 100 meters with or without resting</td>
</tr>
<tr>
<td>6.5</td>
<td>Needs canes, crutches, braces to walk for 20 meters without resting</td>
</tr>
<tr>
<td>7.0</td>
<td>Unable to walk beyond five meters even with aid; mostly confined to a wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours a day</td>
</tr>
<tr>
<td>7.5</td>
<td>Unable to take more than a few steps; restricted to wheelchair; may need aid in transfer; wheels self but cannot carry on in standard wheelchair a full day; may require motorized wheelchair</td>
</tr>
<tr>
<td>8.0</td>
<td>Essentially restricted to bed, chair, or wheelchair, but may be out of bed itself much of the day; retains many self-care functions; generally has effective use of arms</td>
</tr>
<tr>
<td>8.5</td>
<td>Essentially restricted to bed much of day; has some effective use of arms; retains some self-care functions</td>
</tr>
<tr>
<td>9.0</td>
<td>Helpless bed patient; can communicate and eat</td>
</tr>
<tr>
<td>9.5</td>
<td>Totally helpless bed patient; unable to communicate effectively or eat/swallow</td>
</tr>
<tr>
<td>10.0</td>
<td>Death due to MS</td>
</tr>
</tbody>
</table>


REFERENCES:

Revision/Review Date: 10/12/2011
Associated Policy: Prior Authorization of Medications 236.200

NOTE: Clinical reviewer must override criteria when, in his/her professional judgement, the requested item is medically necessary.