Pharmacy Management Drug Policy

SUBJECT: Tysabri ® (natalizumab) Multiple Sclerosis, Crohn's Disease
POLICY NUMBER: PHARMACY-53
EFFECTIVE DATE: 4/08
LAST REVIEW DATE: 2/3/2020

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

DESCRIPTION:

Tysabri is a humanized monoclonal antibody integrin receptor antagonist that inhibits leukocyte adhesion and migration into inflamed tissue. Tysabri has been proven medically effective for the treatment of patients with the following conditions:

Multiple Sclerosis: TYSABRI is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML). When initiating and continuing treatment with TYSABRI, physicians should consider whether the expected benefit of TYSABRI is sufficient to offset this risk.

- Efficacy of this product in primary progressive forms of multiple sclerosis has not been established.

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 CD therapies and inhibitors of TNF-α.

Tysabri is administered as an IV infusion by a healthcare provider during an office visit. Therefore coverage is provided under the **medical benefit** and not the prescription drug benefit. Tysabri is also subject to a strict management program based on the risk of progressive multifocal leukoencephalopathy in 1.66 in 1,000 patients.

****This criteria only applies to Managed Medicaid (MMC)/Child Health Plus (CHP); no prior authorization is requested for lines of business other than MMC/CHP****

POLICY:

Based upon our assessment and review of the peer-reviewed literature, Tysabri has been medically proven to be effective and therefore, **medically necessary** for the treatment of the following FDA-approved diagnoses if specific criteria are met:

A. Multiple Sclerosis:

1. Member must have a diagnosis of relapsing-remitting or relapsing secondary progressive multiple sclerosis **AND**
2. Member must have had a clinical exacerbation or evidence of worsening disease with an adequate trial (minimum 12 weeks each) of at least **TWO** different preferred agents (Avonex, Copaxone, Gilenya, Rebif or Tecfidera)

AND

3. Member must not currently be on combination therapy with any other Multiple Sclerosis disease modifying agent such as Avonex, Rebif, Betaseron, Extavia, Copaxone, Aubagio, Tecfidera or Gilenya **AND**
4. Patients must not be on concurrent immunosuppressive therapy, including mycophenolate, azathioprine, steroids, IVIG due to increased risk of side effects*(See #4 under Policy Guidelines) **AND**

5. Physician office must be approved by the manufacturer (Biogen Idec) to have met the risk management criteria (see #6 in Policy Guidelines)

B. Crohn's Disease: Tysabri has been medically proven to be effective and therefore, **medically necessary** for the treatment of Crohn's disease if all of the following criteria are met

1. Diagnosis of moderately to severely active Crohn's disease made by a gastroenterologist **AND**
2. Moderate to severe disease - Crohn's Disease Activity Index (CDAI) score of 220-450. Typically described as having more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting or significant anemia **AND**
3. Member meets at least **one** of the following criteria
    - **a.** Patient continues to experience disease flare despite complete and adequate therapy with a corticosteroid (such as prednisone or budesonide)

      OR
    - **b.** Treatment with an immunomodulator (such as azathioprine or 6-mercaptopurine) fails to maintain remission in a case of steroid dependent or steroid refractory CD.

      OR
    - **c.** Documentation is provided that azathioprine, 6-mercaptopurine, or methotrexate is not effective, contraindicated, or not tolerated.
4. Must also have documentation of clinical failure (intolerance or lack of effect) to Inflectra AND Entyvio.
5. Authorization period and limitations for patients with Crohn's disease:
    - **a.** Dosing will be authorized at 300mg infused over approximately one hour, every four weeks
    - **b.** Discontinue in patients that have not experienced therapeutic benefit by 12 weeks on induction therapy, and in patients that cannot discontinue chronic steroids within six months of starting therapy. Other than the six month taper prescribers should consider discontinuing Tysabri for patients who require additional steroid use that exceeds three months in a calendar year.

POLICY GUIDELINES:

1. Prior-authorization is subscriber contract dependent.
2. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then

trial of the preferred drug(s) will not be required.
- The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
- The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
- The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
- The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
- The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
- The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.

3. Tysabri is not to be used in immunocompromised patients due to the possible risk of serious infection.
4. Tysabri is contraindicated in patients with current PML or a history of PML
5. The use of Tysabri as a **first line therapy** for the treatment of multiple sclerosis will be assessed on a case by case basis through a letter of medical necessity based on severity of the disease. Coverage will be considered if any of the following are met: ≥2 attacks within the last 18 months, brain stem/cerebellar/or spinal cord disease, greater than 3 gadolinium enhancing lesions with significant clinical exacerbations and/or motor involvement, bilateral optic neuritis, and/or rapid cognitive decline.
6. Patients who are approved for coverage of Tysabri under the medical benefit will be excluded from coverage for immunosuppressants including mycophenolate, 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, sirolimus, methotrexate, and IVIG under the pharmacy benefit or the medical benefit. A 3 – 6 month washout period has been proposed prior to beginning therapy with Tysabri. Aminosalicylates may be continued during treatment with Tysabri. Criteria for coverage of immunosuppressants after Tysabri approval is as follows:
    a. Member must have active Crohn's disease
    b. Member must not currently be on combination therapy with Tysabri
7. Patients who are approved for coverage of Tysabri under the medical benefit will be excluded from the concomitant use of biologics (including Humira, Cimzia or infliximab) under the pharmacy or medical benefit. Criteria for coverage of these agents after Tysabri approval is as follows:
    a. Member must have active Crohn's disease
    b. Member must not currently be on combination therapy with Tysabri

   Coverage of Tysabri is limited to one 300mg IV infusion once every 4 weeks.
8. Physician office must be approved by the manufacturer (Biogen Idec) to have met the risk management criteria. Check eligibility on the Tysabri website:

www.tysabri.com/support/find-a-doctor

9. Patient must be enrolled in the TOUCH program (Tysabri Outreach: Unified Commitment to Health)
10. STRATIFY JCV, the recently FDA approved JCV (John Cunningham Virus) Antibody ELISA test, screens for the presence of antibodies to the JC virus, a risk factor for PML in patients with MS or Crohn's disease who are taking natalizumab. It is recommended that individuals be tested for anti-JCV status prior to treatment or during treatment if antibody status is unknown. Individuals with negative anti-JCV antibody test should be retested periodically.
11. The risk of progressive multifocal leukoencephalopathy (PML) should be assessed at each visit. Individuals with the following 3 risk factors are at highest risk:
    - Antibody test results (presence of anti-JCV antibodies, indicating prior exposure to JCV)
    - Cumulative exposure to natalizumab (risk increases between 2 - 3 years of exposure (>24 doses) and then begins to plateau; data after 6 years is limited)
    - Previous exposure to immunosuppressants (mitoxantrone, azathioprine, methotrexate, cyclophosphamide, and mycophenolate mofetil)
12. The risks and benefits of continuing treatment with Tysabri should be carefully considered in patients who are found to be anti-JCV antibody positive and have one or more additional risk factors.

Approval time periods:

Line of business	**Medical Initial approval**	**Medical recertification**
Medicaid Managed Care/Child Health Plus	6 months	12 months
Commercial/Exchange	Outpatient hospital: 6 months	Outpatient hospital: 6 months
	Home Care/Office Based: 3 years	Home Care/Office Based: 3 years
Medicare	Outpatient hospital: 3 years	Outpatient hospital: 3 years
	Home Care/Office Based: 3 years	Home Care/Office Based: 3 years

Policy Exclusions:

1. Coverage of Tysabri at a dosage higher than 300mg or at a more frequent duration than every 4 weeks is considered experimental and will not be covered.

CODES: Number **Description**

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently

than policy updates.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

HCPCS: J2323 Tysabri (natalizumab)

UPDATES:

Date	Revision
2/2020	Revised
12/2019	Revised
9/2019	Updated
5/2019	P&T Committee Approval
3/2019	Reviewed
12/18	Reviewed
12/17	Revised
9/17	Revised & P&T Approval
8/17	Review
8/16	Review
5/15	Review
12/13	Revised
7/13	Revised
4/13	Revised
2/12	Revised
2/11	Revised
11/10	Revised
10/09	Reviewed
10/08	Revised
4/08	Created

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