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 relapsing-remitting form of multiple sclerosis to decrease the frequency of clinical exacerbations/relapses. Efficacy of this product in primary progressive, secondary progressive and relapsing-progressive forms of multiple sclerosis has not been established. Tysabri is also 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 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.

POLICY:

Based upon FLRx’s assessment and review of the peer-reviewed literature, Tysabri has been medically proven to be effective and therefore, medically necessary for any of the following indications if all of the following criteria are met:

A. Multiple Sclerosis: Tysabri has been medically proven to be effective and therefore, medically necessary for the treatment of the relapsing-remitting form of multiple sclerosis if all of the following criteria are met:

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 with an adequate trial of at least TWO different preferred agents (Avonex, Copaxone, 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 Cellcept, Imuran, 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

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 Remicade
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. Tysabri is not to be used in immunocompromised patients due to the possible risk of serious infection.
3. 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.
4. 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
5. 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 Remicade) 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.
6. Physician office must be approved by the manufacturer (Biogen Idec) to have met the risk management criteria
7. Patient must be enrolled in the TOUCH program (Tysabri Outreach: Unified Commitment to Health)
8. 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.
9. 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
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, SafetyNet and Health Care Reform products only when a contract benefit for the specific service exists.

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)

10 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.

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).

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HCPCS: J2323 Tysabri (natalizumab)

REFERENCES:
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