Policy Title:	Tysbari (natalizumab) (Intravenous)		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	9/12/2018, 12/13/2019, 1/22/2020, 6/10/2021, 1/20/2022, 7/13/2023, 12/07/2023, 01/10/2024, 01/22/2025		

Purpose: To support safe, effective, and appropriate use of Tysbari (natalizumab) in the treatment of Multiple Sclerosis and Crohn's disease.

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

Policy Statement:

Tysbari (natalizumab) is covered under the medical benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:

Coverage of Tysbari (natalizumab) will be reviewed prospectively via the prior authorization process based on criteria below.

Summary of Evidence:

Tysabri (natalizumab) is an integrin receptor antagonist used to treat multiple sclerosis (MS) and Crohn's disease. Clinical trials evaluating its efficacy and safety have demonstrated significant benefits in reducing the frequency of relapses and slowing disease progression in patients with MS. Tysabri has shown superior efficacy compared to placebo and other disease-modifying therapies in reducing the risk of disability progression. The AFFIRM trial showed that Tysabri reduced the annualized relapse rate by 68% compared to placebo in patients with relapsing-remitting MS. Additionally, the SENTINEL trial demonstrated that Tysabri reduced the risk of disability progression by 42% compared to placebo. There is a black box warning for risk of progressive multifocal leukoencephalopathy (PML).

Initial Criteria:

- Patient is at least 18 years of age; AND
- Patient has had anti-JCV antibody testing with ELISA prior to initiating treatment with natalizumab and annually thereafter; AND
- Cannot be used in combination with antineoplastic, immunosuppressant, or immunomodulating agents; AND
- Patient must not have a systemic medical condition resulting in significantly compromised immune system function

- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Multiple Sclerosis (MS):

- Patient is diagnosed with a relapsing form of multiple sclerosis and documented by laboratory report (i.e., MRI); AND
- Must be prescribed by or in consultation with a neurologist; AND
- Used as monotherapy for the treatment of relapsing forms of MS; AND

Crohn's Disease:

- Patient is diagnosed with Crohn's disease by a gastroenterologist; AND
- Prescriber has assessed baseline disease severity utilizing an objective measure/tool; AND
- Patient has had failure, intolerance, or contraindication to infliximab IV or adalimumab therapy for at least 3 months at maximum tolerated doses; AND
- Patient has had failure, intolerance, or contraindication to ustekinumab for at least 6 months at maximum tolerated doses; AND
- Patient is not taking in combination with another biologic drug or immunosuppressant (e.g., 6-mercaptopurine, azathioprine, cyclosporine, methotrexate, etc.) used for Crohn's disease; AND
- Tysabri is prescribed by or in consultation with a gastroenterologist

Continuation of therapy criteria:

- Multiple Sclerosis:
  - Patient is tolerating treatment
  - Patient has annual anti-JCV antibody testing with ELISA
  - Patient has experienced disease improvement or slowing of disease worsening (e.g., no decline in Expanded Disability Status Score [EDSS] or MRI findings) since initiating therapy
- Crohn's disease:
  - Patient is tolerating treatment
  - Patient has annual anti-JCV antibody testing with ELISA
  - For initial renewal only:
    - Patient must show clinical response and remission of disease by 12 weeks
  - For all subsequent renewals:
    - Patient does not require additional steroid use that exceeds three months in a calendar year
    - Disease response as indicated by improvement in signs and symptoms compared to baseline such as endoscopic activity, number of liquid stools, presence and severity of abdominal pain, presence of abdominal mass, body weight compared to IBW, hematocrit, presence of extra intestinal complications, use of anti-diarrheal drugs, and/or an improvement on a disease activity scoring tool [e.g., an

improvement on the Crohn's Disease Activity Index (CDAI) score or the Harvey-Bradshaw Index score]

Coverage durations:

- Initial coverage criteria = 3 months for Crohn's disease and 6 months for MS
- Continuation of therapy = 12 months

Per §§ 42 CFR 422.101, this clinical medical policy only applies to INTEGRITY in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Tysabri was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Tysabri according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

Dosage/Administration:

Indication	Dose	Maximum dose (1 billable unit = 1 mg)
All Indications	300 mg intravenously over one hour every four weeks	300 billable units every 28 days

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable to covered treatment options for multiple sclerosis. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria are provided in the procedure section.

Codes:

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J2323	Injection, natalizumab, 1mg
Q5134	Injection, natalizumab-sztn (tyruko), biosimilar, 1mg

References:

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