Medical Policy

BlueCross BlueShield of Kansas
An Independent Licensee of the Blue Cross and Blue Shield Association

Title: Tysabri (natalizumab)

Prior Authorization Form:
http://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth_1301KS_MDR_Tysabri.pdf
Prime Therapeutics will review Prior Authorization requests

For information concerning Prior Authorization Prescription Drugs:
http://www.bcbsks.com/CustomerService/PrescriptionDrugs/prior_authorization.htm

Link to Drug List (Formulary):
http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.htm

Professional
Original Effective Date: January 1, 2012
Revision Date(s): November 1, 2012; July 8, 2013; October 4, 2013; January 1, 2014
Current Effective Date: January 1, 2014

Institutional
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Revision Date(s): November 1, 2012; July 8, 2013; October 4, 2013; January 1, 2014
Current Effective Date: January 1, 2014

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The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

The intent of the Tysabri (natalizumab) Prior Authorization (PA) program is to appropriately select patients for treatment according to product labeling and/or clinical studies and/or clinical practice guidelines. The PA program will approve Tysabri for patients with Multiple Sclerosis (MS) or Crohn's Disease (CD) who have failed to respond to or have intolerance to preferred first line and conventional therapies used to treat these conditions, who do not have any FDA contraindications to therapy, and with appropriate FDA labeled dosing.

Target Drugs

Tysabri (natalizumab)

FDA Approved Indications and Dosage

FDA Indication(s): As monotherapy for the treatment of relapsing forms of multiple sclerosis (MS) to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations. Efficacy beyond 2 years is unknown. Due to the risk of progressive multifocal leukoencephalopathy (PML), natalizumab is generally recommended for patients who have had an inadequate response to, or are unable to tolerate an alternate MS therapy.

Natalizumab 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 CD therapies and TNF inhibitors. Natalizumab should not be used in combination with immunosuppressants or TNF inhibitors.

Dosing: Dosing for multiple sclerosis and Crohn's disease is 300 mg intravenously every 4 weeks.

POLICY

Prior Authorization Criteria

Initial Evaluation

Tysabri (natalizumab) will be approved when ALL of the following are met:

1. ONE of the following:
    a. The patient is not currently being treated with a disease modifying agent (DMA) for the requested indication (Multiple Sclerosis [MS] or Crohn's Disease [CD])
    OR
    b. The patient is currently being treated with a DMA for the requested indication AND the DMA will be discontinued before starting the requested agent

(evidence of a paid claim within the past 90 days, new claim within the past 120 days **and** physician states the patient is currently taking the requested medication in the past 90 days)

AND

2. The patient does not have any FDA labeled contraindications to therapy with the requested agent.

AND

3. ONE Of the following:
   a. There is documentation that the patient is currently being treated with natalizumab

      OR

   b. ALL of the following:
      1) The patient has an FDA labeled diagnosis for the requested agent

         AND

      2) For MS ONE of the following:
         a) The patient's medication history includes the use of at least 2 preferred agents (i.e. Betaseron, Copaxone, Rebif, or Tecfidera)

            OR

         b) The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to two preferred agents

         AND

      3) For CD BOTH of the following:
         a) ONE of the following:
            i. The patient's medication history includes the use of at least one conventional therapy (e.g. aminosalicylates, metronidazole, ciprofloxacin, corticosteroids, methotrexate, or immunomodulators such as azathioprine or 6-mercaptopurine)

               OR

            ii. The patient has a documented intolerance, FDA labeled contraindications, or hypersensitivity to conventional CD therapy

            AND

         b) ONE of the following:
            i. The patient's medication indicates use of a preferred biologic agent (i.e. adalimumab [Humira]) for the treatment of CD

               OR

            ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the preferred biologic agent for the treatment of CD

AND

4. The prescribed dose is within the FDA approved labeled dosage

Length of Approval: 12 months for MS and
16 weeks for CD

Renewal Evaluation

Tysabri (natalizumab) will be renewed when ALL of the following are met:

1. The patient has been previously approved for the requested therapy through Prime Therapeutics PA process.
   AND
2. The patient has shown clinical benefit with natalizumab
   AND
3. The patient is NOT currently being treated with an additional disease modifying agent (DMA) for the intended FDA labeled indication.
   AND
4. The patient does not have any FDA labeled contraindications to therapy
   AND
5. The prescribed dosage is within the FDA approved labeled dosage

Length of Approval: 12 months

Agent[1]	Contraindications
Tysabri (natalizumab)	Patients who have or have had progressive multifocal leukoencephalopathy (PML). Patients who have had a hypersensitivity reaction to natalizumab.

Contraindicated Concomitant Medications	
Agent	**Contraindicated Therapy**
Tysabri	No concomitant use with any ONE of the following
	natalizumab
	Actemra (Tocilizumab)
	Amevive (Alefacept)
	Arcalyst (Rilonacept)
	Aubagio (Teriflunomide)
	Avonex (Interferon beta-1a)
	Betaseron (Interferon beta-1b)
	Cimzia (Certolizumab)
	Copaxone (Glatiramer)
	Enbrel (Etanercept)
	Extavia (Interferon beta-1b)
	Gilenya (Fingolimod)
	Humira (Adalimumab)
	Ilaris (Canakinumab)
	Kineret (Anakinra)
	Orencia (Abatacept)
	Rebif (Interferon beta-1a)
	Rituxan (Infliximab)
	Simponi (Golimumab)
	Stelara (Ustekinumab)
	Tecfidera (Dimethyl fumarate)

Quantity Limit

Brand (generic)	Quantity Limit
Tysabri® (natalizumab)	
300 mg/15 mL vial	1 vial/28 days

RATIONALE

Multiple Sclerosis

The treatment of MS is multifaceted and includes immunomodulatory therapy and symptom modification. Treatment for an acute relapse includes steroids and plasma exchange for those patients who do not respond to steroid therapy. Disease modifying therapies (DMAs) have been shown to slow the progression of disability and reduce the accumulation of lesions within the brain and spinal cord. There are several agents currently FDA approved to treat relapsing forms of MS. These include interferon beta-1a (Avonex, Rebif), interferon beta-1b (Betaseron, Extavia), glatiramer acetate (Copaxone), natalizumab (Tysabri), mitoxantrone, fingolimod (Gilenya), teriflunomide (Aubagio), and dimethyl fumarate (Tecfidera).[7]

Guidelines from the United States and Europe recommend treatment for RRMS be initiated with either glatiramer or interferon beta (INFβ).[4,5] Natalizumab is generally reserved for patients who have failed to respond to first line agents or for patients who have very progressive disease.

Concurrent use of more than one injectable DMA has been studied in clinical trials. The combinations of INFβ with natalizumab and glatiramer with natalizumab have been studied. Although a beneficial effect was seen (such as improved magnetic resonance imaging (MRI) parameters), there may be more adverse reactions associated with combination therapies. The study with a combination of INFβ and natalizumab was halted due to reported cases of progressive multifocal leukoencephalopathy (PML).[6]

Crohn's Disease

Treatment goals in CD include best control of inflammatory disease with the fewest medication side effects, normal patient function, and growth and nutritional balance in pediatric CD patients. A step wise approach for medical management is the gold standard in CD. Patients with mild disease are typically stepped-up while patients with moderate to severe disease are treated with a step-down approach. Conventional agents include 5-aminosalicyclic acid (5-ASA), antibiotics, 6-mercaptopurine, azathioprine, methotrexate, and budesonide. If patients do not respond to these agents, several biologic agents have FDA approval to treat CD. Surgical interventions are reserved for treating complications and controlling symptoms but surgical resection is not curative.[8]

The American College of Gastroenterology (ACG) practice guidelines for CD in adults (2009)[9] recommend treatment for mild to moderate CD with oral aminosalicylates (mesalamine and sulfasalazine), antibiotics (metronidazole or ciprofloxacin), and corticosteroid treatment (controlled-release budesonide or other conventional corticosteroids).[9,10] For moderate to severe disease, azathioprine or 6-mercaptopurine (6-MP) are effective.[9] Infliximab is recommended by ACG, the American Gastroenterological Association (AGA),and the British Society of Gastroenterology as a second-line treatment option in patients with moderately to severely active, refractory CD (including fistulizing disease).[9,11,12] The 2009 ACG guidelines for CD[9] state

that infliximab, adalimumab, and certolizumab are all effective in the treatment of moderate to severely active CD in patients who have not responded despite complete and adequate therapy with a corticosteroid or an immunosuppressive agent. Natalizumab is effective in patients who have had an inadequate response or are unable to tolerate conventional CD therapy and anti-TNF-α monoclonal antibody therapy.[9]

Safety

Natalizumab and Progressive Multifocal Leukoencephalopathy (PML)

Tysabri (natalizumab) has a boxed warning for increasing the risk of PML, an opportunistic viral infection of the brain that usually leads to death or severe disability. The FDA MedWatch alert on February 5, 2010 notified healthcare professionals and patients that the risk of developing PML increases with the number of natalizumab infusions received. Information about the occurrence of Immune Reconstitution Inflammatory Syndrome (IRIS) in patients who have developed PML and subsequently discontinued natalizumab has also been added to the drug label. IRIS is a rare condition characterized by a severe inflammatory response that can occur during or following immune system recovery, causing an unexpected decline in a patient's condition after return of immune function.[2] Revisions to the drug label and patient *Medication Guide*, with the continued use of the TOUCH Prescribing Program, are intended to maximize the safe use of Tysabri (natalizumab) and the identification of new PML cases.[2] Risk factors and risk stratification for the development of PML have been recommended. The risk factors identified include treatment duration with natalizumab of greater than 2 years, prior immunosuppressive use (e.g. mitoxantrone, azathioprine, methotrexate, cyclophosphamide, or mycophenolate mofetil) and JCV virus seropositive. Patients with all 3 risk factors have an estimated PML risk of 11/1,000 users.[3]

Natalizumab is contraindicated in patients who have had or who have PML and in patients with hypersensitivity to natalizumab. The most common adverse events (incidence ≥10%) in MS include headache, fatigue, urinary tract infection, lower respiratory tract infection, gastroenteritis, vaginitis, depression, pain in extremity, abdominal discomfort, diarrhea, and rash. Common adverse events in CD include headache, upper respiratory tract infection, nausea, and fatigue.[1]

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J2323 Injection, natalizumab, 1 mg

REVISIONS

01-01-2014	Policy added to the bcbsks.com web site. Published on 12-02-2014. A stand alone policy was developed from policy language previously contained in the Multiple Sclerosis Agents (also addresses Tysabri's use in Crohn's disease) medical policy.

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