Department:	Pharmacy Management	**Original Approval:**	01/20/2016
Policy #:	PM126	**Last Approval:**	03/14/2019
Title:	Natalizumab (Tysabri®)		
Approved By:	UM Committee		

REQUIRED CLINICAL DOCUMENTATION FOR REVIEW

Documentation required to determine medical necessity for Natalizumab (Tysabri): History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Diagnosis -Age - Medication list (current and past) to include start and end dates of previous trials for all biologics and disease-modifying agents -Prescribed by or in consultation with a neurologist, gastroenterologist or specialist as indicated -Labs/diagnostics -Dosing and duration requested.

BACKGROUND

Tysabri is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis (MS).[1] 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. PML is opportunistic viral infection of the brain caused by the John Cunningham virus (JCV) that usually leads to death or severe disability. Efficacy of Tysabri in relapsing MS was established in two pivotal clinical trials.[2-3] Additional clinical data are also available. 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 tumor necrosis factor (TNF)-α.[1,4-6] Tysabri should not be used in combination with immunosuppressants (e.g., azathioprine, 6-mercaptopurine, cyclosporine, methotrexate [MTX]) or inhibitors of TNFα. The recommended dose of Tysabri is 300 mg by IV infusion over approximately 1 hour every 4 weeks.[1] Tysabri is available as a preservative-free solution in single-use vials containing 300 mg of Tysabri in 15 mL (20 mg/mL). This concentrated solution must be diluted before IV administration in 100 mL of 0.9% sodium chloride injection. It should not be given IV push or by bolus injection.

Risk Evaluation and Mitigation Strategy (REMS)

Tysabri is available only through a special restricted distribution Risk Evaluation and Mitigation Strategy (REMS) program called the TOUCH® Prescribing Program, which requires registration by the prescribers, patients, infusion centers, and pharmacies associated with infusion centers.[1] Tysabri must be administered only to patients enrolled in and who meet all the conditions of the TOUCH Prescribing Program. Tysabri's MS indication is for monotherapy because it is unknown how combination use with other immune modifying drugs could impact its safety.[1] Tysabri is associated with an increased risk of PML.

For Crohn's disease, Tysabri should not be used with concomitant immunosuppressants or TNFα inhibitors.[1] Also in Crohn's disease, the drug should be discontinued if the patient has not had therapeutic benefit by 12 weeks of induction therapy. For patients with Crohn's disease who initiate Tysabri while on chronic oral corticosteroids, steroid tapering should be started as soon as a therapeutic benefit of Tysabri has occurred. If these patients cannot be tapered off oral corticosteroids within 6 months of starting Tysabri, Tysabri must be discontinued. Prescribers should also consider discontinuing Tysabri in patients who require additional steroid use > 3 months in a calendar year to control their Crohn's disease.

Multiple Sclerosis (MS)

MS is a chronic demyelinating, disabling disease of the central nervous system (CNS) characterized by recurrent and progressive neurologic dysfunction.[8] MS lesions occur in many different parts of the CNS and the symptoms and clinical course of the disease are highly variable. Some common signs and symptoms of the disease include vision problems (e.g., nystagmus), ambulation problems, pain, fatigue, spasticity, cognitive dysfunction, depression, ataxia, sensory loss, bladder disturbances, bowel dysfunction, dizziness, and vertigo. Most people with MS are diagnosed between the ages of 20 and 50 years, but MS can manifest in young children and older adults. Approximately 400,000 people are living with MS in the US and approximately 200 people are newly diagnosed weekly.

Four different clinical courses of MS have been delineated.[8] A relapse is defined as the development of new or recurring symptoms lasting at least 24 hours and separated from a previous attack by at least 1 month. Relapsing-remitting MS (RRMS) is characterized by acute attacks usually followed by almost complete recovery with limited progression. Disease progression is minimal between attacks. Approximately 85% of people are initially diagnosed with RRMS. Secondary progressive MS (SPMS) begins as relapsing-remitting course but the disease transitions in many patients to a steadily progressive form with increased loss of function. Of the 85% of patients who initially have RRMS, more than 50% will develop SPMS within 10 years and 90% within 25 years. Primary progressive MS (PPMS) is noted by a steady decline in function from the onset without noted relapses. Around 10% of patients are diagnosed with PPMS. Progressive-relapsing MS (PRMS) starts with disease progression at onset with occasional acute relapses and continued disease progression. Only a small minority of patients (< 5%) have PRMS. About 10% of the MS population has a benign disease course, which is generally determined retrospectively. Among those with relapsing forms of MS, the severity, duration, and frequency of relapses vary widely among patients. The Expanded Disability Scale Score (EDSS) is the scale most often used to assess neurologic disability and evaluates cerebellar, pyramidal, brainstem, sensory, bowel, bladder, visual, and mental functional systems on a scale that ranges from 0 (normal neurologic examination) to 10 (death due to MS). Magnetic resonance imaging (MRI) evaluations are used to assess current MS disease activity, as well as to monitor for permanent neurologic damage.

Other Disease-Modifying Drug Therapies for Multiple Sclerosis

Many medications are indicated for use in relapsing forms of MS including self-injected therapies such as interferon beta products (e.g., Avonex® [interferon beta-1a for intramuscular {IM} injection], Rebif® [interferon beta-1a for subcutaneous {SC} injection],[8] Betaseron®/Extavia® (interferon beta-1b for SC injection] and Plegridy™ [peginterferon beta-1a injection])[9-13] and glatiramer acetate products (Copaxone®, 20 mg/mL and 40 mg/mL, generics).[14-17] Although some differences in efficacy have been observed in clinical trials among the interferon beta products, in general, these self-injectable MS

therapies appear to reduce the annualized relapse rate (ARR) by approximately one-third.[18] Oral therapies indicated in relapsing forms of MS include Aubagio® (teriflunomide tablets),[20] Gilenya™ (fingolimod capsules),[21] and Tecfidera™ (dimethyl fumarate delayed-release capsules).[22] Therapies administered by IV infusion include Lemtrada® (alemtuzumab injection for IV use)[24] and and Ocrevus® (ocrelizumab injection for IV use).[26] Ocrevus is also indicted for use in patients with progressive forms of multiple sclerosis (MS).

Crohn's Disease, Adults

According to 2008 American College of Gastroenterology (ACG) guidelines on management of Crohn's disease in adults, patients with moderate-severe Crohn's disease are treated with prednisone 40 to 60 mg/day until symptoms are resolved or weight gain is resumed (usually 7 to 28 days).[28] Infection or abscess is treated with antibiotics or drainage. For maintenance therapy, azathioprine or 6-mercaptopurine have been beneficial after induction therapy with corticosteroids. Parenteral methotrexate 25 mg/week is effective for steroid-dependent and steroid-refractory Crohn's disease. The TNFα antagonists, Cimzia, Humira, and an infliximab product (e.g., Remicade, Inflectra), are effective for moderate to severe active Crohn's disease in those who have not responded despite complete and adequate therapy with a corticosteroid or an immunosuppressive agent. Monotherapy with an infliximab product or an infliximab product plus azathioprine is more effective than azathioprine in patients with mild to moderate Crohn's disease who do not respond to first-line therapy with mesalamine and/or corticosteroids. Humira has been effective in patients who have not received other biologics and in those who lost response to an infliximab product (e.g., Remicade, Inflectra). Cimzia, Humira, and an infliximab product may be used as alternatives to steroids in selected patients with Crohn's disease who have contraindications to corticosteroids or who not desire steroid therapy. Tysabri is effective in moderate to severe active Crohn's disease and active inflammation (e.g., elevated C-reactive protein level) who have an inadequate response or are unable to tolerate conventional Crohn's disease therapies and TNF antagonists. The 2013 ACG guidelines on use of thiopurines, methotrexate, and TNFα antagonists biologics in Crohn's disease do not address use of Tysabri.[29] These guidelines have not been updated since the approvals of Entyvio and Stelara for bowel conditions.

Documentation: Documentation is required for initiation of therapy where noted in the criteria as [documentation required]. Documentation may include, but is not limited to, chart notes and magnetic resonance imaging (MRI) reports.

DEFINITIONS

None.

INDICATIONS/CRITERIA

Medicaid Members	***Tysabri is not considered for approval for Relapsing Forms of Multiple Sclerosis unless member has tried and failed TWO preferred products,***

	including: Avonex, Betaseron, Copaxone, Gilenya, Rebif, Tecfidera. Tysabri is included in the WA HCA Single Preferred drug list. *Document if member meets this criteria, which medications were tried, and deny if criteria is not met. Otherwise, continue to clinical criteria below.*
Medicare Members	***Step-utilization of Part D drugs not required.*** ***Continue to criteria for approval below.***

Coverage of Tysabri is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. Relapsing Form of Multiple Sclerosis (MS).

Criteria. *The patient must meet one of the following criteria (A or B)*:

A) Initial Therapy. Approve for 1 year if the patient meets all of the following criteria (i, ii, iii and iv):

i. The patient is ≥ 18 years of age; AND

ii. The patient has a relapsing form of multiple sclerosis (MS) [relapsing forms of MS are relapsing-remitting MS {RRMS}, secondary-progressive MS with relapses {SPMS}, and progressive-relapsing MS {PRMS}]; AND

iii. Tysabri is prescribed by or in consultation with a physician who specializes in the treatment of multiple sclerosis (MS) and/or a neurologist; AND

iv. The patient meets ONE of the following (a or b):

a. According to the prescribing physician the patient has had an inadequate response or is unable to tolerate ONE disease-modifying agent used for MS (e.g., Avonex [interferon beta-1a for intramuscular {IM} injection], Rebif [interferon beta-1a for subcutaneous {SC} injection], Betaseron [interferon beta-1b for SC injection], Extavia [interferon beta-1b for SC injection], Copaxone [glatiramer acetate injection for SC use], Glatopa [glatiramer acetate injection for SC use], Plegridy [peginterferon beta-1a SC injection], Gilenya [fingolimod capsules], Aubagio [teriflunomide tablets], Tecfidera [dimethyl fumarate delayed-release capsules], Lemtrada [alemtuzumab injection for intravenous use], or Ocrevus [ocrelizumab injection for IV use]); OR

b. According to the prescribing the physician the patient has highly-active or aggressive multiple sclerosis by meeting one of the following (1, 2, 3, or 4):

1. The patient has demonstrated rapidly-advancing deterioration(s) in physical functioning (e.g., loss of mobility/or lower levels of ambulation, severe changes in strength or coordination) **[documentation required]**; OR

2. Disabling relapse(s) with suboptimal response to systemic corticosteroids **[documentation required]**; OR

3. Magnetic resonance imaging [MRI] findings suggest highly-active or aggressive multiple sclerosis (e.g., new, enlarging, or a high burden of T2 lesions or gadolinium-enhancing lesions) **[documentation required]**; OR

4. Manifestations of multiple sclerosis-related cognitive impairment **[documentation required]**; OR

B) Patients currently receiving Tysabri. Approve for 1 year if the patient meets all of the following criteria (i, ii, and iii):

i. The patient is ≥ 18 years of age; AND
ii. The patient has a relapsing form of multiple sclerosis (MS) (relapsing forms of MS are relapsing-remitting MS [RRMS], secondary-progressive MS with relapses [SPMS], and progressive-relapsing MS [PRMS]): AND
iii. Tysabri is prescribed by, or in consultation with, a physician who specializes in the treatment of MS and/or a neurologist.

Tysabri is indicated for the treatment of adults with relapsing forms of MS.[1] Tysabri therapy is considered by some experts for rapidly-worsening MS.[30] A practice guideline recommendation regarding disease-modifying agents for adults with MS from the American Academy of Neurology (2018) states to consider Tysabri for patients with MS who have highly active disease.[19]

Dosing in Multiple Sclerosis (MS) in Adults.
Dosing must meet the following: 300 mg IV infusion over 1 hour every 4 weeks.[1]

Duration of Therapy in Multiple Sclerosis (MS): Indefinite if the conditions for coverage and dosing continue to be met (see above).

Labs/Diagnostics. None required.

2. Crohn's Disease.

Criteria. *The patient must meet the following criteria (A or B):*

A) Initial Therapy. Approve for 3 months if the patient meets all of the following criteria (i, ii, iii, or iv):

i. The patient is ≥ 18 years of age; AND
ii. Patient has moderately to severely active Crohn's disease with evidence of inflammation, that is, has an elevated C-reactive protein; AND
iii. Tysabri is prescribed by or in consultation with a gastroenterologist; AND
iv. Patient has tried at least two of the following agents for Crohn's disease: Humira (adalimumab for subcutaneous [SC] injection], Cimzia (certolizumab pegol for SC injection), an infliximab product (for example, Remicade [infliximab for IV infusion], Inflectra [infliximab-dyyb IV infusion, Renflexis [infliximab-abda IV infusion]), Entyvio™ (vedolizumab injection for IV use), or Stelara® (ustekinzumab for SC injection or for IV infusion) for at least 2 months each and had an inadequate response or was intolerant to these agents; AND

B) For patients currently receiving Tysabri. Approve for 1 year if the patient meets all of the following criteria (i, ii, and iii):

i. The patient is ≥ 18 years of age; AND

ii. The patient has had a response (e.g., reduced number of liquid/soft stools, reduced abdominal pain, less use of antidiarrheal agents) to Tysabri, as determined by the prescribing physician; AND
iii. Tysabri is prescribed by or in consultation with a gastroenterologist.

Tysabri is indicated for reducing 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.[1]

Dosing in Crohn's Disease.
Dosing must meet the following: 300 mg IV infusion over one hour every 4 weeks.[1]

The approved dose of Tysabri in Crohn's disease is a 300 mg IV infusion over one hour every 4 weeks.[1] If the patient has not experienced therapeutic benefit by 12 weeks of induction, then Tysabri should be discontinued. In patients with Crohn's disease who start Tysabri while on chronic oral corticosteroids, steroids should be tapered as soon as there is a therapeutic benefit from Tysabri. If the patient cannot be tapered off of oral corticosteroids within 6 months of starting Tysabri, then Tysabri should be discontinued. Also, consideration should be given to discontinuing Tysabri in patients who require additional steroid therapy in excess of 3 months in a calendar year to control their Crohn's disease.

Duration of Therapy in Crohn's Disease. Indefinite if the conditions for coverage and dosing continue to be met (see above).

Labs/Diagnostics. None required.

Conditions Not Recommended for Approval
Tysabri has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Children with Multiple Sclerosis (MS) or Crohn's disease.** Tysabri is not indicated in pediatric patients with MS or Crohn's disease who are < 18 years of age.[1] There have been case series reports of use of Tysabri in adolescents aged 12 to 17 years with RRMS who were refractory to other agents.[27-28] Long-term risks of using Tysabri in children are not known. Interferon beta and Copaxone are the two most frequently used disease modifying therapies used in pediatric patients with RRMS in the US.[29] Limited information is available on use of Tysabri in adolescents with Crohn's disease.[30]

2. **Concurrent Use of Tysabri with an Immunosuppressant Agent in Patients with Crohn's Disease.** Tysabri should not be given in combination with an immunosuppressant agent (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or MTX) or with a TNFα inhibitor (e.g., an infliximab product [such as Remicade, Inflectra], Humira, Cimzia).[1] Tysabri is not indicated in combination

with Entyvio or Stelara. Ordinarily, patients who are receiving chronic immunosuppressant or immunomodulatory therapy or who have systemic medical conditions resulting in significantly compromised immune function should not take Tysabri.[1] Aminosalicylates may be continued during therapy with Tysabri. Tysabri can be started in patients on chronic oral corticosteroids, but patients should be tapered off corticosteroids.

3. **Current Use of Tysabri with Other Disease-Modifying Agents Used for Multiple Sclerosis (MS) or with an Immunosuppressant in Patients with MS.** Tysabri should not be given in combination with other disease-modifying agents used for MS (e.g., Betaseron/Extavia, Rebif, Copaxone/Glatopa, Avonex, Lemtrada, Plegridy, Zinbryta, Gilenya, Aubagio, Tecfidera) or with an immunosuppressant such as mitoxantrone, cyclophosphamide, Ocrevus (ocrelizumab injection for IV use), Rituxan® (rituximab injection for IV infusion), Campath® (alemtuzumab injection for IV infusion), azathioprine, MTX, or mycophenolate mofetil. Tysabri is only indicated as monotherapy due to an increased risk of PML.[1] Ordinarily, patients with MS who are receiving chronic immunosuppressant or immunomodulatory therapy or who have systemic medical conditions resulting in significantly compromised immune function should not take Tysabri.

4. **Immune Compromised Patients with Multiple Sclerosis (MS) or Crohn's Disease.** Patients with a medical condition that results in significantly compromised immune system function such as human immunodeficiency virus (HIV) infection, leukemia, lymphoma, or organ transplant should not ordinarily be treated with Tysabri.[1]

5. **Primary Progressive (Chronic Progressive) Multiple Sclerosis (MS).** The safety and efficacy of Tysabri have not been studied in patients with primary progressive (chronic progressive) MS. Tysabri is indicated in patients with relapsing forms of MS.[1]

6. **Ulcerative Colitis.** Efficacy data with use of this product are limited.[31]

7. Coverage is not recommended for circumstances *not* listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

SPECIAL CONSIDERATIONS

None.

LIMITATIONS/EXCLUSIONS

Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

PRODUCT LINE	LINK TO CERTIFICATE OF COVERAGE
MEDICARE ADVANTAGE	http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides
WASHINGTON APPLE HEALTH	http://chpw.org/our-plans/apple-health/
INTEGRATED MANAGED CARE	http://chpw.org/our-plans/apple-health/

Citations & References

References

1. Tysabri® injection for intravenous use [prescribing information]. Cambridge, MA: Biogen; Revised April 2018.
2. Polman CH, O'Connor PW, Havrdova E, et al, for the AFFIRM Investigators. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. N Engl J Med. 2006;354:899-910.
3. Rudick RA, Stuart WH, Calabresi PA, et al, for the SENTINEL Investigators. Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. N Engl J Med. 2006;354:911-923.
4. Sandborn WJ, Colombel JF, Enns R, et al, for the International Efficacy of Natalizumab as Active Crohn's Therapy (ENACT-1) and the Evaluation of Natalizumab as Continuous Therapy (ENACT-2) Trial Group. Natalizumab induction and maintenance therapy for Crohn's disease. N Engl J Med. 2005;353:1912-1925.
5. Targan SR, Feagan BG, Fedorak RN; International Efficacy of Natalizumab in Crohn's Disease Response and Remission (ENCORE) Trial Group. Natalizumab for the treatment of active Crohn's disease: results of the ENCORE Trial. Gastroenterology. 2007;132:1672-1683.
6. Feagan BG, Sandborn WJ, Hass S, et al. Health-related quality of life during natalizumab maintenance therapy for Crohn's disease. Am J Gastroenterol. 2007;102:2737-2746.
7. US Food and Drug Administration. FDA Drug Safety Communication: Risk of Progressive Multifocal Leukoencephalopathy (PML) with the use of Tysabri (natalizumab). Updated February 5, 2010. Available at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm199872.htm Accessed on December 15, 2017.
8. Clinical bulletin. Information for health professionals. Overview of multiple sclerosis. Rosalind Kalb and Nancy Reitman. © 2012 National Multiple Sclerosis Society.
9. Avonex® intramuscular injection [prescribing information]. Cambridge, MA: Biogen; March 2016.
10. Plegridy™ subcutaneous injection [prescribing information]. Cambridge, MA: Biogen, Inc.; July 2016.
11. Rebif® subcutaneous injection [prescribing information]. Rockland, MA and New York, NY: EMD Serono and Pfizer; November 2015.
12. Betaseron® injection for subcutaneous use [prescribing information]. Whippany, NJ: Bayer; April 2016.

13. Extavia® injection for subcutaneous use [prescribing information]. East Hanover, NJ: Novartis; May 2016.
14. Copaxone® injection for subcutaneous use [prescribing information]. Kansas City, MO: Teva Neuroscience; August 2016.
15. Glatiramer acetate injection 20 mg/mL [prescribing information]. Morgantown, WV: Mylan Pharmaceuticals; February 2017.
16. Glatiramer acetate injection 40 mg/mL [prescribing information]. Morgantown, WV: Mylan Pharmaceuticals; April 2017.
17. Glatopa® injection for subcutaneous use [prescribing information]. Princeton, NJ: Sandoz Inc; April 2016.
18. McGraw CA, Lublin FD. Interferon beta and glatiramer acetate therapy. Neurotherapeutics. 2013;10:2-18.
19. Zinbryta® injection for subcutaneous use [prescribing information]. Cambridge, MA and North Chicago, IL: Biogen and AbbVie; August 2017.
20. Aubagio® tablets [prescribing information]. Cambridge, MA: Genzyme (a Sanofi Corporation); November 2016.
21. Gilenya® capsules [prescribing information]. East Hanover, NJ: Novartis; February 2016.
22. Tecfidera® delayed-release capsules [prescribing information]. Cambridge, MA: Biogen Idec; January 2017.
23. O'Connor PW, Oh J. Disease-modifying agents in multiple sclerosis. Handb Clin Neurol. 2014;122:465-501.
24. Lemtrada® injection for intravenous use [prescribing information]. Cambridge, MA: Genzyme Corporation; December 2017.
25. Mitoxantrone injection [prescribing information]. Irvine, CA: Teva Medicines, Inc.; May 2012.
26. Ocrevus™ injection for intravenous infusion [prescribing information]. San Francisco, CA: Genentech, Inc (a Member of the Roche Group); March 2017.
27. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis: principles and current evidence. July 2016. Available at: http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/DMT_Consensus_MS_Coalition.pdf Accessed on December 15, 2017.
28. Lichtenstein GR, Hanauer SB, Sandborn WJ; and The Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol. 2009;104:465-483.
29. Terdiman JP, Gruss CB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute guideline on the use of thiopurines, methotrexate, and anti-TNF-α biologic drugs for the induction and maintenance of remission in inflammatory Crohn's disease. Gastroenterology. 2013;145:1459-1463.
30. Boster A, Edan G, Frohman E, et al; Multiple Sclerosis Clinical Research Center, Department of Neurology, Wayne State University School of Medicine. Intense immunosuppression in patients with rapidly worsening multiple sclerosis: treatment guidelines for the clinician. Lancet Neurol. 2008;7:173-183.
31. Simone M, Chitnis T. Use of disease-modifying therapies in pediatric MS. Curr Treat Options Neurol. 2016;18:36.
32. Ghezzi A, Pozzilli C, Grimalde LM, et al; Italian MS Study Group. Natalizumab in pediatric multiple sclerosis: results of a cohort of 55 cases. Mult Scler. 2013;19:1106-1112.
33. Yeh EA, Waubant E, Krupp LB, et al; for the National Network of Pediatric MS Centers of Excellence. Multiple sclerosis therapies in pediatric patients with refractory multiple sclerosis. Arch Neurol. 2011;68:437-444.

	34. Hyams JS, Wilson DC, Thomas A, et al; International Natalizumab CD305 Trial Group. Natalizumab therapy for moderate to severe Crohn disease in adolescents. J Pediatr Gastroenterol. Nutr. 2007;44:185-191. 35. Gordon FH, Hamilton MI, Donoghue S, et al. A pilot study of treatment of active ulcerative colitis with natalizumab, a humanized monoclonal antibody to alpha-4 integrin. Aliment Pharmacol Ther. 2002;16:699-705. 36. Zhovtis Ryerson L, Frohman TC, Foley J, et al. Extended interval dosing of natalizumab in multiple sclerosis. J Neurol Neurosurg Psychiatry. 2016;87:885-889. 37. Weinstock-Guttman B, Hagemeier J, Kavak KS, et al. Randomised natalizumab discontinuation study: taper protocol may prevent disease reactivation. J Neurol Neurosurg Psychiatry. 2016;87:937-943. OTHER REFERENCES UTILIZED 38. Bloomgren G, Richman S, Hotermans C, et al. Risk of natalizumab-associated progressive multifocal leukoencephalopathy. N Engl J Med. 2012;366:1870-1880. 39. Freedman MS, Selchen D, Arnodl DL, et al; Canadian Multiple Sclerosis Working Group. Treatment optimization in MS: Canadian MS Working Group updated recommendations. Can J Neurol Sci. 2013;40:307-323. 40. Huppke P, Stark W, Zürcher C, et al. Natalizumab use in pediatric multiple sclerosis. Arch Neurol. 2008;65:1655-1658. 41. Hutchinson M, Kappos L, Calabresi PA, et al; AFFIRM and SENTINEL Investigators. The efficacy of natalizumab in patients with relapsing multiple sclerosis: subgroup analyses of AFFIRM and SENTINEL. J Neurol. 2009;256:405-415. 42. Scott FI, Osterman MT. Natalizumab for Crohn's disease: down but not out. Clin Gastroenterol Hepatol. 2015;13:1926-1928. 43. Yeh EA, Weinstock-Guttman B. Natalizumab in pediatric multiple sclerosis patient. Ther Adv Neurol Disord. 2010;5:293-299.

CFR		
WAC	284-43-2050	
RCW		
Contract Citation	☐ WAH	
	☐ IMC	
	☐ MA	
Other Requirements		
NCQA Elements		

Revision History

Revision Date	Revision Description	Revision Made By
01/13/2016	New	Kelly Force; Yusuf Rashid, RPh
01/20/2016	Approval	MMLT
01/12/2017	No revisions	Fran McGaugh
01/13/2017	Approval	MMLT
07/24/2017	Criteria completely updated and revised	Michael Sporck, Pharmacy Intern Sophia Yun, PharmD

07/25/2017	Approved	MMLT
03/09/2018	Reassigned from UM137 to PM126	Cindy Bush
05/22/2018	Updated, added LOB box	Gary Deng, Pharmacy Student Catherine Vu, PharmD
06/14/2018	Approval	UM Committee
03/06/2019	Revised. Defined highly active/aggressive disease. Minor formatting changes.	Ivan Figueira, PharmD
03/14/2019	Approval	UM Committee