

Multiple Sclerosis Therapy

To Initiate a Coverage Review, Call 1 800 753-2851

Impacted Medications	
➤ Interferon beta-1b (Betaseron®)	➤ Glatiramer acetate (Copaxone®)
➤ Interferon beta-1b (Extavia®)	➤ Natalizumab (Tysabri®)
➤ Interferon beta-1a (Avonex®)	
➤ Interferon beta-1a (Rebif®)	

What Is Multiple Sclerosis?
<ul style="list-style-type: none"> ➤ Multiple sclerosis (MS) is believed to be an autoimmune disease of the nervous system where myelin, a natural insulating material that surrounds nerve fibers in the brain and spinal cord, is damaged (this is referred to as demyelination). ➤ Demyelination results in the disruption of nerve impulses to and from the brain, leading to clinical manifestations such as optic neuritis (vision changes), muscle weakness or lack of coordination, slurred speech, gait difficulties, bladder and bowel problems, and partial or complete paralysis. ➤ Disease progression is associated with relapses, remissions, and possible immobility. ➤ Diagnosis of definite MS is made after the occurrence of two demyelinating events separated by time, (at least 1 month), and space, meaning damage in different areas of the brain. Advances in imaging technology, such as magnetic resonance imaging (MRI), has helped facilitate diagnosis. In cases where the diagnosis is uncertain or where a differential diagnosis is still warranted, analysis of the patients' cerebral spinal fluid may be useful as well. ➤ Clinical management involves prevention of relapses, management of acute relapses, and providing symptomatic relief. Steroids are first-line therapy for acute exacerbations. Immunomodulatory and immunosuppressive agents are used as chronic therapy to reduce relapse rates and delay the progression of disease. Treatment can be initiated immediately after the first demyelinating event to delay the development of clinically definite MS. Management of MS requires long-term treatment. ➤ Natalizumab is also indicated for the induction and maintenance of remission in patients with moderate to severe Crohn's disease: a chronic, episodic inflammatory condition of the gastrointestinal (GI) tract, which mostly occurs in persons between the ages of 15 and 35, and often presents with cramp-like pain in the lower right abdomen, diarrhea, rectal bleeding and weight loss. ➤ Untreated, Crohn's disease can lead to small bowel stricture or obstruction requiring surgery. Fistulas may also occur as a consequence of CD in the areas of worst inflammation. ➤ Currently there is no cure for Crohn's disease, however, symptomatic treatment often includes aminosalicylates (5-ASAs), corticosteroids (prednisone and methylprednisolone), immunomodulators (azathioprine or 6-mercaptopurine), biologic agents (Humira®, Remicade®, and Tysabri®), and antibiotics to help control inflammation and heal fistulas.

Types of Multiple Sclerosis	
Relapsing-remitting	Characterized by oscillation between acute attacks and full or partial recovery. Partial recovery is associated with some residual deficit following an acute attack.
Progressive-relapsing	Characterized by initial relapsing-remitting disease followed by progression at variable rate, which can include occasional relapses and minor remissions or plateaus (disease progression not increasing or decreasing).
Secondary progressive	Characterized by progression from onset of MS, but with no clear acute relapses with or without full recovery.
Primary progressive	Characterized by progression of disability without any remissions or even occasional minor improvements.

Medications to Treat MS	How They Work
Interferon beta-1b (Betaseron®) Interferon beta-1b (Extavia®) Interferon beta-1a (Avonex®) Interferon beta-1a (Rebif®)	<ul style="list-style-type: none"> • Interferons act as immunomodulatory/anti-inflammatory agents to potentially reduce the frequency and severity of exacerbations in patients with MS. • Interferons can reduce disease burden (i.e., amount of plaque) in the central nervous system and may prolong exacerbation-free periods. • Betaseron® and Extavia® are the same medicinal products (interferon beta-1b); both are manufactured at the same facility.
Glatiramer acetate (Copaxone®)	<ul style="list-style-type: none"> • Glatiramer is a mixture of amino acids (the building blocks of proteins) that exert their action by becoming a target site of attack thereby suppressing the immune-mediated attacks on myelin.
Natalizumab (Tysabri®)	<ul style="list-style-type: none"> • Natalizumab is a monoclonal antibody drug designed to block the movement of certain immune cells across the blood-brain barrier. It blocks movement by attaching to $\alpha\beta 1$-integrins, proteins found on the surface of immune T-cells that enable the cells to cross the blood-brain barrier. This action interrupts the

	<p>inflammatory process, which may slow the progression of the disease.</p> <ul style="list-style-type: none"> • Natalizumab has demonstrated the ability to reduce relapse rates. • Patients receiving other immunosuppressive agents should not receive concurrent therapy with natalizumab due to the possibility of increasing the risk of infection. The only beta interferon that has been studied concurrently with natalizumab is Avonex[®]. Patients who had experienced one or more relapses while on Avonex[®] monotherapy saw a reduction in relapses from the addition of natalizumab. It is not known whether other beta interferons or glatiramer will decrease the frequency of relapses if used with natalizumab. • Natalizumab has been reintroduced to the market with a black-box warning for progressive multifocal leukoencephalopathy (PML). The risk of PML may be increased in immune-compromised patients or patients receiving immunosuppressive therapy such as beta interferons. Natalizumab is now only available through the TOUCH[™] Prescribing Program.
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Rationale for Prior Authorization
To reduce exposure to cost associated with use where the effectiveness of MS drug therapy has not been demonstrated (e.g., concurrent use of a beta interferons with glatiramer or natalizumab).

Benefit Design
Coverage will be determined through a prior authorization process for all claims.

Prior Authorization Criteria
<p>Coverage is provided for beta interferons and glatiramer acetate (Copaxone[®]) in accord with the following:</p> <ol style="list-style-type: none"> 1. Coverage provided for treatment at time of first demyelinating event to delay development or progression to MS. 2. Coverage provided for relapsing-remitting, secondary progressive or progressive-relapsing MS. Coverage is not provided for primary progressive MS. 3. Coverage provided for situations in which there is functional status that can be preserved. Patient must still either be able to walk at least a few steps or alternatively must have some functional arm/hand use consistent with performing activities of daily living. 4. Combination therapy with interferon beta and glatiramer acetate is not covered. <p><u>Coverage duration:</u></p> <ul style="list-style-type: none"> • Coverage is provided for 12 months and may be renewed. <p>Coverage is provided for natalizumab (Tysabri[®]) in accord with the following:</p> <ol style="list-style-type: none"> 1. Coverage is provided for use in patients ≥ 18 years of age for the treatment of relapsing-remitting MS who have failed or been intolerant of beta interferons or Copaxone[®]. <ul style="list-style-type: none"> • Natalizumab (Tysabri[®]) is <u>not</u> covered in the presence of concurrent Copaxone[®] therapy, chronic use of other immunosuppressive therapy [e.g., Avonex[®]], or in immune-compromised patients. 2. Coverage is provided for use in patients ≥ 18 years of age for induction or maintenance of remission in patients with moderate to severe Crohn's disease. <ul style="list-style-type: none"> • In situations where the patient has experienced failure or intolerance to previous treatment with Humira[®] and Remicade[®]. • Natalizumab (Tysabri[®]) is <u>not</u> covered in the presence of TNF-α inhibitor therapy. <p><u>Coverage duration:</u></p> <ul style="list-style-type: none"> • Coverage is provided for 6 months for relapsing-remitting MS. • Coverage is provided for 3 months for induction or maintenance of remission in patients with moderate to severe Crohn's disease. • Coverage is renewable for 12 months in situations where treatment is continuing to provide clinical benefit.

References
<ul style="list-style-type: none"> ➤ Cook SD, et al. <i>Handbook of Multiple Sclerosis</i>. Third edition. 2001. ➤ Data on file. Extavia (Interferon beta-1b) – Comparison with other interferon beta-1b products. East Hanover, NJ: Novartis Pharmaceuticals Corporation, 2009. ➤ Goodin DS, Arnason BG, Coyle PK, Frohman EM, Paty DW. The use of mitoxantrone (Novantrone) for the treatment of multiple sclerosis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. <i>Neurology</i>. Nov 2003;61:1332-1338. ➤ Jacobs LD, Beck RW, Simon JH, et al. Intramuscular Interferon Beta-1a Therapy Initiated During a First Demyelinating Event in Multiple Sclerosis. <i>N Engl J Med</i>. 2000;343(13):898-904. ➤ National Collaborating Centre for Chronic Conditions. <i>Multiple Sclerosis</i>. National clinical guidelines for diagnosis and management in primary and secondary care. London (UK): National Institute for Clinical Excellence (NICE);2004:197 ➤ Noseworthy JH et al. Multiple sclerosis. <i>N Engl J Med</i>. 2000;343(13):938-952.

- Product Information: Interferon Beta-1a (Rebif® – Serono 2004)
- Product Information: Interferon Beta-1a (Avonex® – Biogen 2004)
- Product Information: Interferon beta-1b (Betaseron® – Bayer 2008)
- Product Information: Interferon beta-1b (Extavia® – Novartis 2009)
- Product Information: Glatiramer acetate (Copaxone® – Aventis 2002)
- Product Information: Mitoxantrone (Novantrone® – Serono 2006)
- Product Information: Natalizumab (Tysabri® – Biogen 2008)
- Sandborn WJ, et al. Natalizumab Induction and Maintenance Therapy in Crohn's Disease. *N Engl J Med.* 2005 Nov 3;353(18):1912-1925.
- Targan SR et al. Natalizumab and the treatment of active Crohn's disease: Results of the ENCORE Trial. *Gastroenterology.* 2007 May;132(5):1672-1683.