

**Pharmacy Prior Authorization
Multiple Sclerosis – Clinical Guideline**

Copaxone® (glatiramer acetate)	Glatiramer acetate	Glatopa® (glatiramer acetate)
Tecfidera® (dimethyl fumarate)	Avonex® (interferon beta-1a)	Mitoxantrone
Extavia® (interferon beta-1b)	Gilenya® (fingolimod)	Mayzent® (siponimod)
Aubagio® (teriflunomide)	Plegridy® (peginterferon beta-1a)	Vumerity (diroximel fumarate)
Ocrevus™ (ocrelizumab)	Lemtrada® (alemtuzumab)	
Tysabri® (natalizumab)	Mavenclad (cladribine)	

Preferred Products:

Copaxone 40mg/mL, Tecfidera

Non-preferred products:

Require documentation to support trial and failure, or contraindication with two preferred agents

General Authorization Criteria for all Agents:

- Member is 18 years of age or older for all agents except Gilenya (10 years of age or older)
- Medication is prescribed by a Neurologist
- Other disease modifying multiple sclerosis therapies (not including Ampyra) will be, or have been discontinued

Additional Criteria for Specific Medications:

• **INJECTABLE AGENTS**

- **Copaxone 40mg, Glatopa (20mg glatiramer acetate), Extavia (interferon beta-1b), Avonex (interferon beta-1a)**
 - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or active secondary progressive multiple sclerosis), or
 - Member has clinically isolated syndrome suggestive of multiple sclerosis (for example, persons who have experienced first clinical episode, and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis)
- **Plegridy (peg-interferon beta-1a)**
 - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or active secondary progressive multiple sclerosis) or
 - Member has clinically isolated syndrome suggestive of multiple sclerosis (for example, persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis)
 - Member had inadequate response, intolerable side effects, or contraindication to two (2) formulary agents, one of which must be an interferon or glatiramer acetate

• **ORAL AGENTS**

- **Aubagio (teriflunamide)**
 - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or active secondary progressive multiple sclerosis), or
 - Member has clinically isolated syndrome suggestive of multiple sclerosis (for example, persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis)
 - Females of reproductive potential are not pregnant prior to start of therapy, and will be using effective contraception during treatment
 - All the following labs have been completed within the last six (6) months

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- Complete Blood Count
 - Liver Function Tests and bilirubin levels
 - Tuberculin skin test
- Gilenya (fingolimod)
- Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or active secondary progressive multiple sclerosis), or
 - Member has clinically isolated syndrome suggestive of multiple sclerosis (for example, persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis)
 - All the following labs have been completed within the last six (6) months
 - Complete Blood Count
 - Liver Function Tests and bilirubin levels
 - Electrocardiogram evaluation performed
 - Ophthalmic examination
 - Member has documented history of chicken pox, or has had the varicella zoster vaccination, or has evidence of immunity (positive antibodies)
 - There is no history of any of the following:
 - Myocardial Infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or class III/IV heart failure within the past six (6) months
 - Corrected QT (QTc) greater than or equal to 500 msec
 - History of Mobitz type II (2nd or 3rd degree atrioventricular block), or sick sinus syndrome, unless member has a pacemaker
 - Treatment with Class Ia or Class III anti-arrhythmic drugs
- Mayzent (siponimod)
- Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or active secondary progressive multiple sclerosis), or
 - Member has clinically isolated syndrome suggestive of multiple sclerosis (for example, persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis)
 - Member has been tested for CYP2C9 variants to determine CYP2C9 genotype, and is not positive for CYP2C9*3/*3
 - All the following labs have been completed within the last six (6) months
 - Complete Blood Count
 - Liver Function Tests and bilirubin levels
 - Electrocardiogram evaluation performed
 - Ophthalmic examination
 - Member has documented history of chicken pox, or has had the varicella zoster vaccination, or has evidence of immunity (positive antibodies)
 - There is no history of any of the following:
 - Myocardial Infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or class III/IV heart failure within the past six (6) months
 - History of Mobitz type II (2nd or 3rd degree atrioventricular block), or sick sinus syndrome, unless member has a pacemaker

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- Mavenclad (cladribine)
 - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or active secondary progressive multiple sclerosis)
 - Member does not have a diagnosis of clinically isolated syndrome
 - Baseline (within 3 months) MRI scan is obtained prior to starting treatment course due to risk of progressive multifocal leukoencephalopathy (PML)
 - Females of reproductive potential are not pregnant prior to start of therapy, and will be using effective contraception during treatment
 - Member is not infected with Human Immunodeficiency Virus and has no active chronic infections (for example, hepatitis or tuberculosis), or is breastfeeding (during treatment or for 10 days after last dose)
 - Lifetime maximum of 2 courses (4 cycles) of therapy
- Tecfidera (dimethyl fumarate), Vumerity (diroximel fumarate)
 - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or active secondary progressive multiple sclerosis), or
 - Member has clinically isolated syndrome suggestive of multiple sclerosis (for example, persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis)
 - All the following labs have been completed within the last 6 months:
 - Complete blood count
 - Liver function tests and bilirubin levels
- **INFUSIONS**
 - Ocrevus (ocrelizumab)
 - Member has been screened for Hepatitis B and does not have an active Hepatitis B infection
 - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or active secondary progressive multiple sclerosis), or
 - Member has clinically isolated syndrome suggestive of multiple sclerosis (for example, persons who have experienced a first clinical episode, and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis) and
 - Member had inadequate response, intolerable side effects, or contraindication to two (2) formulary agents, one of which must be an interferon or glatiramer acetate, or
 - Diagnosis of Primary-Progressive Multiple Sclerosis (PPMS)
 - Lemtrada (alemtuzumab)
 - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or active secondary progressive multiple sclerosis)
 - Will not exceed five (5) days of treatment the first year, and three (3) days of treatment the 2nd year. (subsequent treatment courses of 12mg per day on 3 consecutive days (36mg total dose) may be administered, as needed, at least 12 months after the last dose of any prior treatment course)
 - Member is not infected with Human Immunodeficiency Virus (HIV)
 - All the following have been completed prior to initiating treatment:
 - Complete blood count
 - Serum creatinine levels
 - Complete any necessary immunizations at least 6 weeks prior to treatment
 - History of varicella, or has had the varicella zoster vaccination, or has evidence of immunity (positive antibodies)

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- Member has been screened for tuberculosis. If screening was positive for latent tuberculosis, member has received treatment for latent tuberculosis
- Thyroid function test such as a thyroid stimulating hormone level (TSH)
- Member had inadequate response, intolerable side effects, or contraindication to two (2) formulary agents, one of which must be an interferon or glatiramer acetate
- Tysabri (natalizumab)
 - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or active secondary progressive multiple sclerosis), or
 - Member has clinically isolated syndrome suggestive of multiple sclerosis (for example, persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis)
 - Anti-JCV (John Cunningham virus) antibody test (ELISA [enzyme-linked immunosorbent assay]) has been completed (those with positive anti-JCV [John Cunningham Virus] antibody have a higher risk for developing progressive multifocal leukoencephalopathy [PML]).
 - Member had inadequate response, intolerable side effects, or contraindication to two (2) formulary agents, one of which must be an interferon or glatiramer acetate
- Mitoxantrone
 - Member has one of the following diagnoses:
 - Secondary (chronic) progressive multiple sclerosis
 - Progressive relapsing multiple sclerosis
 - Worsening relapsing-remitting multiple sclerosis to reduce neurologic disability and/or frequency of clinical relapse
 - Mitoxantrone is not indicated for treatment of primary progressive multiple sclerosis
 - Cumulative lifetime dose is less than 140 mg/m²
 - Member had inadequate response, intolerable side effects, or contraindication to two (2) formulary agents, one of which must be an interferon or glatiramer acetate
 - All the following labs were completed within the last six (6) months:
 - LVEF (left ventricular ejection fraction) greater than 50% (not below lower limit of normal)
 - Absolute neutrophil count (ANC) greater than 1500 cells/mm³
 - CBC (complete blood count) including platelets
 - LFTs (liver functions tests)

Initial Approval:

- All injections: 12 months
- All orals: six (6) months
- Tysabri and mitoxantrone: three (3) months
- Ocrevus: six (6) months
- Lemtrada: 12 months
- Mavenclad is limited to a total of 2 courses per lifetime

Renewal Approval:

- Requires documentation and lab results to support response to treatment, and that there is no serious toxicity as a result of treatment
 - for example, LVEF [left ventricular ejection fraction], CBC [complete blood count], ANC [absolute neutrophil count], ECG [electrocardiogram]
- All orals: 12 months

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- Lemtrada: 12 months
- Mitoxantrone: three (3) months
- Tysabri and Ocrevus: six (6) months
- Mavenclad is limited to a total of 2 courses per lifetime

Additional information:

- Examples of treatment failure (over 1 year period of using disease-modifying therapies):
 - 1 or more relapses
 - Magnetic resonance imaging (MRI) lesion progression (for example, increase in T1, T2, or gadolinium lesions)
 - Worsening disability or Expanded Disability Status Scale (EDSS) score

*Dosing Table serves as a guidance and not always updated. Please confirm details in Clinical Pharmacology or the PI

Multiple Sclerosis Agent	Max Dose	Strength	Frequency and Quantity
Aubagio	14mg/day	7mg; 14mg	Daily: Up to 30 tablets in 30 days
Gilenya	Children weighing more than 40kg & adults: 0.5 mg/day Children weighing less than 40kg: 0.25mg	0.25mg, 0.5mg	Daily: Up to 30 capsules in 30 days
Tecfidera	480mg/day	120mg 240mg	Up to 14 delayed release capsules or 1 starter pack in 30 days (for taper) Up to 60 delayed release capsules in 30 days
Vumerity	462 mg twice daily	231mg	Initial: 231 mg twice daily Maintenance: 462 mg twice daily
Avonex	30mcg/week	30mcg/0.5ml	Up to 4 syringes per month
Copaxone/Glatopa Glatiramer acetate,	20mg/day 40mg three times per week	20mg/ml, 40mg/ml	Daily (subcutaneous [SQ]): 20 mg, up to 30 ml per month 20mg: QLL = 1ml per day 3 times per week (subcutaneous [SQ]): 40 mg- up to 12 ml per 28 days 40mg: QLL = 12ml per 28 days
Extavia	250mcg every other day	0.3mg	Up to 15 syringes per 30 days
Plegridy	125mcg every 14 days	125mcg/0.5ml	Up to 2 syringes per month
Lemtrada	12mg/day for 5 days	12mg/1.2ml	Year 1: 5 days of 12mg (60mg total: 5 vials) Year 2 and beyond: 3 days of 12mg (36mg total: 3 vials)
Tysabri	300mg every 4 weeks	300mg/15ml	Up to 1 vial per month

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Rebif	44mcg every 48 hours	22mcg/0.5ml,44mcg/0.5ml	Three times a week (subcutaneous [SQ]):22mcg-44 mcg. Titration 4.2 ml/28 days, Regular injectable 6ml/28days
Mitoxantrone	Lifetime cumulative dose limit of (140 mg/m ²)	2mg/ml	Every 3 months (intravenous [IV]):12 mg/m ²
Mavenclad	Lifetime cumulative dosage of 3.5 mg/kg	10mg	<u>Course 1/cycle 1</u> : start any time <u>Course 1/cycle 2</u> : 23 – 27 days after last dose of course 1/cycle 1 <u>Course 2/cycle 1</u> :at least 34 weeks after last dose of course 1/cycle 2 <u>Course 2/cycle 2</u> : 23 – 27 days after last dose of course 2/cycle 1
Ocrevus	600mg every 6 months	300mg/10ml	300mg intravenous [IV] infusion followed by another 300mg 2 weeks later. Subsequent doses 600mg every 6 months.
Mayzent	2mg/day	0.25mg; 2mg	Daily: Up to 30 tablets in 30 days

Forms of Multiple Sclerosis:

Form	Description
Relapsing-Remitting Multiple Sclerosis	Most common disease course is characterized by clearly defined attacks of worsening neurologic function. These attacks also called relapses, flare-ups or exacerbations are followed by partial or complete recovery periods (remissions), during which symptoms improve partially or completely and there is no apparent progression of disease. Approximately 85 percent of people with multiple sclerosis are initially diagnosed with relapsing-remitting multiple sclerosis
Secondary Progressive Multiple Sclerosis	The name for this course comes from the fact that it follows after the relapsing-remitting course. Most people who are initially diagnosed with Relapsing-Remitting Multiple Sclerosis will eventually transition to Secondary Progressive Multiple Sclerosis, which means that the disease will begin to progress more steadily (although not necessarily more quickly), with or without relapses.
Primary-Progressive Multiple Sclerosis	Primary-Progressive Multiple Sclerosis is characterized by steadily worsening neurologic function from the beginning. Although the rate of progression may vary over time with occasional plateaus and temporary, minor improvements, there are no distinct relapses or remissions. About 10 percent of people with multiple sclerosis are diagnosed with Primary-Progressive Multiple Sclerosis.

References:

1. National Multiple Sclerosis Society. Treating MS. <http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=16103>. Accessed Sept 28, 2015

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2. Owens, GM, Olvey, EL, Skrepnek G, Pill, M. Perspective for Managed Care Organizations on the Burden of Multiple Sclerosis and the Cost-Benefit of Disease Modify Therapies. <http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=16103>. Assessed Oct 2, 2015.
3. Goodin DS, Frohman EM, Garman GP et al. Disease modifying therapies in multiple sclerosis: report of the therapeutics and technology assessment subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology*. 2002; 58:169-78.
4. National Institute for Health and Clinical Excellence (NICE). Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis. URL: www.nice.org.uk. Available from the Internet. Issued 2007 August. Accessed Oct 4 2015.
5. Luzzio, Christopher, MD; Chief Editor: B. Mark Keegan, MD. Multiple Sclerosis Treatment & Management. <http://emedicine.medscape.com/article/1146199-treatment#d10>. Accessed August 29, 2015.
6. Clinical Policy Bulletin: Multiple Sclerosis – Specialty Pharmacy Clinical Policy Bulletins Aetna Non-Medicare Prescription. http://www.aetna.com/products/rxnonmedicare/data/2015/CNS/multiple_sclerosis.html. Accessed September 19, 2019.
7. National Multiple Sclerosis Society. Treating MS. <http://www.nationalmssociety.org/Treating-MS/Medications> <http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=16103>. Accessed Aug 16, 2017
8. The use of Disease Modifying Therapies in Multiple Sclerosis. http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed August 28, 2017.
9. Tysabri® [package insert]. Biogen Inc., Cambridge, MA. Revised August 2019. https://www.tysabri.com/content/dam/commercial/tysabri/pat/en_us/pdf/tysabri_prescribing_information.pdf. Accessed September 18, 2019.
10. Lemtrada® [package insert]. Genzyme Corporation, Cambridge, MA. Revised July 2019. <http://products.sanofi.us/lemtrada/lemtrada.html>. Accessed September 18, 2019.
11. Rebif® [package insert]. EMD Serono, Inc., Rockland, MA. Revised July 2019. <https://www.emdserono.com/content/dam/web/corporate/non-images/country-specifics/us/pi/rebif-pi.pdf>. Accessed September 17, 2019.
12. Avonex® [package insert]. Biogen Inc., Cambridge, MA. Revised August 2019. https://www.avonex.com/content/dam/commercial/avonex/pat/en_us/pdf/Avonex_US_Prescribing_Information.pdf. Accessed September 17, 2019.
13. Betaseron® [package insert]. Bayer Healthcare Pharmaceuticals Inc., Whippany, NJ. Revised August 2019. https://labeling.bayerhealthcare.com/html/products/pi/Betaseron_PI.pdf. Accessed September 17, 2019.
14. Plegridy® [package insert]. Biogen Inc., Cambridge, MA. Revised July 2019. https://www.plegridy.com/content/dam/commercial/multiple-sclerosis/plegridy/pat/en_us/pdf/plegridy-prescribing-information.pdf. Accessed September 17, 2019.
15. Extavia® [package insert]. Novartis Pharmaceuticals Corporation, East Hanover, NJ. Revised August 2019. <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/extavia.pdf>. Accessed September 17, 2019.
16. Aubagio® [package insert]. Genzyme Corporation, Cambridge, MA. Revised July 2019. <http://products.sanofi.us/Aubagio/Aubagio.html>. Accessed September 17, 2019.
17. Gilenya® [package insert]. Novartis Pharmaceuticals Corporation, East Hanover, NJ. Revised August 2019. <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/gilenya.pdf>. Accessed September 17, 2019.
18. Tecfidera® [package insert]. Biogen Inc., Cambridge, MA. Revised July 2017. https://www.tecfidera.com/content/dam/commercial/multiple-sclerosis/tecfidera/pat/en_us/pdf/full-prescribing-info.pdf. Accessed September 17, 2019.
19. Copaxone® [package insert]. Teva Pharmaceuticals USA, Inc., North Wales, PA. Revised July 2019. <https://www.copaxone.com/globalassets/copaxone/prescribing-information.pdf>. Accessed September 17, 2019.
20. Glatopa® [package insert]. Sandoz Inc., Princeton, NJ. Revised July 2019. <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5f01e40a-b6f6-40fb-b37c-3d06f1428e86>. Accessed September 17, 2019.
21. Ocrevus® [package insert]. Genentech, Inc., South San Francisco, CA. Revised July 2019. https://www.gene.com/download/pdf/ocrevus_prescribing.pdf. Accessed September 17, 2019.
22. Mitoxantrone [package insert]. Hospira Inc., Lake Forest, IL. Revised May 2018. <http://labeling.pfizer.com/ShowLabeling.aspx?id=4536>. Accessed September 17, 2019.

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23. Mayzent® [package insert]. Novartis, East Hanover, NJ. Revised March 2019.
<https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/mayzent.pdf>. Accessed September 19, 2019.
24. Mavenclad® [package insert]. Merck KGaA, Darmstadt, Germany. Revised April 2019. <https://www.emdserono.com/us-en/pi/mavenclad-pi.pdf>. Accessed January 17, 2020.
25. Vumerity® [package insert]. Biogen Inc., Cambridge, MA. Revised October 2019.
https://www.vumerity.com/content/dam/commercial/vumerity/pat/en_us/pdf/vumerity-prescribing-information.pdf. Accessed January 17, 2020.
26. Rae-Grant A, Day GA, Marrie RA, et al. American Academy of Neurology. Practice guideline: Disease-modifying therapies for adults with multiple sclerosis. <https://n.neurology.org/content/90/17/777>. Accessed September 19, 2019.
27. Rae-Grant A, Day GA, Marrie RA, et al. American Academy of Neurology. AAN Summary of Practice Guideline for Clinicians. Practice guideline: Disease-modifying therapies for adults with multiple sclerosis. <https://www.aan.com/Guidelines/Home/GetGuidelineContent/900>. Accessed September 19, 2019.