Aetna Better Health®

Pharmacy Prior Authorization
Multiple Sclerosis – Clinical Guideline

Copaxone®(glatiramer acetate)	Glatiramer acetate	**Glatopa** (glatiramer acetate)
Rebif/Rebidose® (interferon beta-1a)	**Extavia®** (interferon beta-1b)	**Avonex®** (interferon beta-1a)
Betaseron® (interferon beta-1b)	**Aubagio®** (teriflunomide)	**Plegridy®** (peginterferon beta-1a)
Tecfidera® (dimethyl fumarate)	**Gilenya®** (fingolimod)	Mitoxantrone
Tysabri® (natalizumab)	**Lemtrada®** (alemtuzumab)	**Ocrevus™** (ocrelizumab)

Preferred Product:
Glatiramer, Glatopa, Copaxone (40mg), Extavia, Rebif, Aubagio, Tecfidera, Gilenya, and Avonex are the preferred Multiple Sclerosis (MS) agents. Non-preferred product will be considered with documentation to support trial and failure or contraindication to 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 (MS) 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), **Rebif/Rebidose** (interferon beta-1a), and **Avonex** (interferon beta-1a)
        - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or secondary progressive multiple sclerosis) or
        - Member has Clinically Isolated Syndrome suggestive of multiple sclerosis (MS) (for example, persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis (MS))

    (Note: Glatopa is the generic form of Copaxone 20mg, the glatiramer acetate 20 mg and the brand Copaxone 40mg are preferred)

    - **Betaseron** (Interferon beta-1b)
        - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or secondary progressive multiple sclerosis) or
        - Member has Clinically Isolated Syndrome suggestive of multiple sclerosis (MS) (for example, persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis (MS))
        - Member had an inadequate response, intolerable side effects, or a contraindication to two formulary agents, one of which must be an interferon or glatiramer acetate

    - **Plegridy** (peg-interferon beta-1a),
        - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or secondary progressive multiple sclerosis)

- Member had an inadequate response, intolerable side effects, or a contraindication to two 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 secondary progressive multiple sclerosis) or
    - Member has Clinically Isolated Syndrome suggestive of multiple sclerosis (MS) (for example, persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with multiple sclerosis (MS))
    - All of the following labs have been completed within the last six (6) months
      - Complete Blood Count (CBC)
      - Liver Function Tests (LFT's) and bilirubin levels
      - Tuberculin skin test
  - **Gilenya** (fingolimod)
    - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or secondary progressive multiple sclerosis)
    - All of the following labs have been completed within the last six (6) months
      - Complete Blood Count (CBC)
      - Liver Function Tests (LFT's) and bilirubin levels
      - Electrocardiogram (EKG) 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 (MI), unstable angina, stroke, or transient ischemic attack (TIA), decompensated heart failure requiring hospitalization within the past six (6) months
      - Corrected QT (QTc) greater than or equal to 500 msec, history of Mobitz type II (2^{nd} or 3^{rd} degree atrioventricular (AV) block) or sick sinus syndrome,
      - Class III/IV heart failure,
      - Treatment with Class Ia or Class III anti-arrhythmic drugs

  - **Tecfidera** (dimethyl fumarate)
    - Diagnosis of relapsing form of multiple sclerosis (for example, relapsing-remitting or secondary progressive multiple sclerosis)
    - All of the following labs have been completed within the last 6 months
      - Complete blood count (CBC)
      - Liver function tests (LFTs) 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 secondary progressive multiple sclerosis) and

- Member had an inadequate response, intolerable side effects, or a contraindication to two 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 secondary progressive multiple sclerosis)
  - Will not exceed five (5) days of treatment the first year and three (3) days of treatment the 2nd year
  - Member is not infected with Human Immunodeficiency Virus (HIV)
  - All of the following have been completed prior to initiating treatment:
    - Complete blood count (CBC)
    - 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)
  - Member had an inadequate response, intolerable side effects, or a 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 secondary progressive 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 an inadequate response, intolerable side effects, or a contraindication to two formulary agents, one of which must be an interferon or glatiramer acetate

- **Mitoxantrone**
  - Member has one of the following diagnoses:
    - Secondary (chronic) progressive (SPMS)
    - Progressive relapsing (PRMS)
    - Worsening relapsing-remitting multiple sclerosis to reduce neurologic disability and/or frequency of clinical relapse
  - Cumulative lifetime dose is less than 140 mg/m^2
  - Member had an inadequate response, intolerable side effects, or a contraindication to two formulary agents, one of which must be an interferon or glatiramer acetate
  - All of the following labs were completed within the last six (6)months:
    - LVEF (left ventricular ejection fraction) greater than 50% (not below the lower limit of normal)
    - Absolute neutrophil count (ANC) greater than 1500 cells/mm3

Initial Approval Duration:
All injections: Indefinite

All orals: six (6) months
Tysabriand mitoxantrone: three (3) months
Ocrevus: six (6) months
Lemtrada: 12 months (two (2) years maximum allowed)

Renewals:
Requires documentation and lab results to support response to treatment (for example, LVEF [left ventricular ejection fraction], CBC [complete blood count], ANC [absolute neutrophil count], ECG [electrocardiogram])
All orals: Indefinite
Lemtrada: 12 months (two [2] year maximum allowed)
Mitoxantrone: three (3) months
Tysabri and Ocrevus: six (6) months

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 guideance and not always updated. Please confirm details in Clinical Pharmacology or the PI.

Multiple Sclerosis (MS) 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
Avonex	30mcg/week	30mcg/0.5ml	Up to 4 syringes per month
Betaseron	250mcg/every other day	0.3mg	Up to 15 syringes per month
Copaxone/Glatopa	20mg/day 40mg three times per week	20mg/ml, 40mg/ml	Daily (subcutaneous [SQ]): 20 mg, up to 30 ml per month 3 times per week (subcutaneous [SQ]): 40 mg- up to 12 ml per month

Extavia	250mcg every other day	0.3mg	Up to 15 syringes per month
Plegridy	125mcg every 14 days	125mcg/0.5ml	Up to 2 syringes per month
Rebif	44mcg every 48 hours	22mcg/0.5ml,44mcg/0.5ml	Three times a week (subcutaneous [SQ]):22mcg-44 mcg.
Lemtrada	12mg/day for 5 days	12mg/1.2ml	Year 1: 5 days of 60mg (total: 5 vials) Year 2: 3 days of 36mg (total: 3 vials)
Tysabri	300mg every 4 weeks	300mg/15ml	Up to 1 vial per month
Mitoxantrone	Lifetime cumulative dose limit of (140 mg/m2	2mg/ml	Every 3 months (intravenous [IV]):12 mg/m^2
Ocrevus	600mg every 6 months	300mg/10ml	300mg intravenous [IV] infusion followed by another 300mg 2 weeks later. Subsequent doses 600mg every 6 months.

Forms of Multiple Sclerosis (MS):

Form	Description
Relapsing-Remitting Multiple Sclerosis (RRMS)	the 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 (SPMS)	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 (RRMS) will eventually transition to Secondary Progressive Multiple Sclerosis (SPMS), which means that the disease will begin to progress more steadily (although not necessarily more quickly), with or without relapses.
Primary-Progressive Multiple Sclerosis (PPMS)	Primary-Progressive Multiple Sclerosis (PPMS) 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 (PPMS).

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