AETNA BETTER HEALTH®
Prior Authorization guideline for Multiple Sclerosis Agents

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

Preferred Product(s):
Glatiramer (Glatopa), Copaxone (40 mg), Extavia, Rebif, Aubagio, Tecfidera, Gilenya and Avonex are the preferred Multiple Sclerosis (MS) agents. Non-preferred products will be considered with documentation to support trial and failure or contraindication to 2 preferred agents.

Authorization guidelines

Discontinuation of treatment of other MS therapies is required before initiating new MS therapy, except for Ampyra.

For patients who have the following:
1. Patient is 18 years of age or older (except for Lemtrada and Zinbryta)
2. Medication is prescribed by a Neurologist
3. Other disease modifying MS therapies (not including Ampyra) will be, or have been discontinued
4. Meet the additional requirements for the requested drug as noted in the following:

Injectable Agents

Copaxone/Glatopa (glatiramer acetate), Extavia (interferon-beta1b), and Avonex (interferon-beta1a)

- Patient has a diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis) OR
- Patient has Clinically Isolated Syndrome suggestive of MS (e.g., persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with MS)
Rebif/Rebifose (interferon-beta1a)
- Diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis)

Betaseron (interferon-beta1b)
- Diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis)
- OR Member has clinically isolated syndrome suggestive of Multiple Sclerosis (e.g., persons who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with MS)
- Patient has had an inadequate response, intolerable side effects, or a contraindication to 2 formulary agents, one of which must be an interferon or glatiramer acetate

Plegridy (peg-interferon-beta1a),
- Diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis)
- Member has had an inadequate response, intolerable side effects, or a contraindication to 2 formulary agents, one of which must be an interferon or glatiramer acetate

Zinbryta (daclizumab)
- Patient has a diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis)
- Current lab results to support serum transaminase levels (ALT and AST)
- The member does not have pre-existing hepatic disease or hepatic impairment, or history of autoimmune hepatitis or other autoimmune condition involving the liver
- Patient has had an inadequate response, intolerable side effects, or a contraindication to 2 formulary agents, one of which must be an interferon or glatiramer acetate

Oral Agents

Ampyra (dalfampridine)
May be approved when the following criteria are met:
- Prescribed by, or in consultation with a neurologist or physical medicine and rehabilitation specialist
- Patient is 18 years of age or older
- Diagnosis of multiple sclerosis with impaired walking ability defined as a baseline 25-ft walking test between 8 and 45 seconds OR Expanded Disability Status Scale (EDSS) between 4.5 and 6.5
- Patient is stabilized on disease modifying therapy for MS (i.e., no recent exacerbations) OR had an inadequate response/intolerance/contraindication to disease modifying therapies
- Patient is NOT wheelchair-bound
- Patient does not have a history of seizures
- Patient does not have moderate to severe renal impairment (Crcl < 50 ml/min)

Additional Information:
Ampyra is NOT covered for members with the following criteria:
- Use not approved by the FDA; AND
The use is unapproved and not supported by the literature or evidence as an accepted off-label use.

Quantity Limit: 2 tablets per day

Approval Duration:
Initial Approval:
• 2 months

Renewal:
• 1 year Patient had an improvement in walking speed or other objective measure of walking ability since starting Ampyra.

Aubagio (teriflunamide)
- Diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis)
- All of the following labs within the last 6 months except as noted
  o CBC
  o LFT’s and bilirubin levels
  o Negative pregnancy if female within previous 1 month
  o Recent Tuberculin skin test

Gilenya (fingolimod)
- Diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis)
- All of the following labs within the last 6 months, except as noted
  o CBC
  o LFT’s and bilirubin levels
  o Negative pregnancy if female, within previous 1 month
  o EKG performed
  o Ophthalmic examination
- Documentation of positive antibodies VZV (history of Chicken pox or vaccination at least one month before starting treatment)
- There is no history of MI, unstable angina, stroke, or TIA within the past 6 months

Tecfidera (dimethyl fumarate)
- Diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis)
- CBC done within the past 6 months

Infusion Agents

Ocrevus (ocrelizumab)
- Member has been screened for Hep B and does not have an active Hep B infection
- Diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis) and

Last Revised: 10/2017
Previous PARP Approval: 11/2017
Current PARP Approval: 1/2018
Member had an inadequate response, intolerable side effects, or a contraindication to 2 formulary agents, one of which must be an interferon or glatiramer acetate or
- Diagnosis of PPMS

**Lemtrada** (alemtuzumab)
- Patient is 17 years of age and older
- Diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis)
- Will not exceed 5 days of treatment the first year and 3 days of treatment the 2nd year
- Not infected with HIV
- Trial and failure of or contraindication to 2 formulary agents, one of which must be an interferon or glatiramer acetate

**Tysabri** (natalizumab)
- Diagnosis of relapsing form of multiple sclerosis (i.e. relapsing-remitting or secondary progressive multiple sclerosis)
- Anti-JCV antibody test (ELISA) performed (those with positive anti-JCV antibody have a higher risk for developing progressive multifocal leukoencephalopathy (PML))
- Trial and failure of or contraindication to 2 formulary agents, one of which must be an interferon or glatiramer acetate
- Tysabri may be considered as a first line therapy in individuals with relapsing forms of multiple sclerosis who exhibit particularly aggressive initial course of disease and in whom the potential benefit is felt to outweigh the risk. Patients with a poor prognosis/aggressive disease include those with a heavy T2 lesion load, lesions in brain stem, cerebellum, and spinal cord.

**Mitoxantrone**
- Diagnosis is secondary (chronic) progressive (SPMS), progressive relapsing (PRMS), or worsening relapsing-remitting multiple sclerosis to reduce neurologic disability and/or frequency of clinical Relapse
- Cumulative dose is less than 140 mg/m²
- All of the following labs within the last 6 months:
  - LVEF (left ventricular ejection fraction) > 50% (not below the lower limit of normal)
  - ANC > 1500 cells/mm³

**Authorization and Limitations**

**Approval Duration:**
- All injections: Indefinite
- Tysabri- 3 months
- Lemtrada-12 months (2 years maximum allowed)
- Mitoxantrone-3 months

**Renewal:**
- Documentation and lab results to support response to treatment (i.e., LVEF, CBC, ANC, ECG, etc.)
- Lemtrada-12 months (2 year maximum allowed)
- Mitoxantrone-3 months
- Tysabri and Ocrevus- 6 months

**Last Revised:** 10/2017
**Previous PARP Approval:** 11/2017
**Current PARP Approval:** 1/2018
### Additional Information:

<table>
<thead>
<tr>
<th>MS Agent</th>
<th>Max Dose</th>
<th>Strength</th>
<th>Frequency and Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampyra</td>
<td>20 mg/day</td>
<td>10mg</td>
<td>10 mg twice daily</td>
</tr>
<tr>
<td>Aubagio</td>
<td>14 mg/day</td>
<td>7mg; 14mg</td>
<td>Daily: Up to 30 tablets in 30 days</td>
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<tr>
<td>Avonex</td>
<td>30 mcg/week</td>
<td>30 mcg/0.5ml</td>
<td>Up to 4 syringes per 28 days</td>
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<tr>
<td>Betaseron</td>
<td>250 mcg/QOD</td>
<td>0.3mg</td>
<td>Up to 15 syringes per month</td>
</tr>
<tr>
<td>Copaxone/Glatopa</td>
<td>20 mg/day</td>
<td>20-40mg/ml</td>
<td>Daily (SQ): 20 mg, up to 30 ml per month</td>
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<tr>
<td></td>
<td>40 mg/week</td>
<td></td>
<td>3x week (SQ): 40 mg- up to 12 ml per 28 days</td>
</tr>
<tr>
<td>Extavia</td>
<td>250 mcg/QOD</td>
<td>0.3mg</td>
<td>Up to 15 syringes per month</td>
</tr>
<tr>
<td>Gilenya</td>
<td>0.5 mg/day</td>
<td>0.5mg</td>
<td>Daily: Up to 30 capsules in 30 days</td>
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<tr>
<td>Lemtrada</td>
<td>12 mg/day x 5 days</td>
<td>12mg/1.2ml</td>
<td>Up to 5 vials per year</td>
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<td></td>
<td></td>
<td></td>
<td>Year 1: 5 days of 60mg</td>
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<td>Year 2: 3 days of 36mg</td>
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<tr>
<td>Mitoxantrone</td>
<td>Lifetime cumulative dose limit of approximately 8–12 doses over 2–3 years (140 mg/m2)</td>
<td>12 mg/m²</td>
<td>Every 3 months (IV):12 mg/m²</td>
</tr>
<tr>
<td>Ocrevus</td>
<td>600mg every 6 months</td>
<td>300mg/250ml</td>
<td>300mg IV infusion followed by another 300mg 2 weeks later. Subsequent doses 600mg every 6 months.</td>
</tr>
<tr>
<td>Plegridy</td>
<td>125mcg/q14 days</td>
<td>125 mcg/0.5ml</td>
<td>Up to 2 syringes per 28 days</td>
</tr>
<tr>
<td>Rebif</td>
<td>44 mcg/q48 hrs</td>
<td>22mcg-44mcg/0.5ml</td>
<td>Three times a week (SQ):22mcg-44 mcg.</td>
</tr>
<tr>
<td>Tecfidera</td>
<td>480 mg/day</td>
<td>120 mg</td>
<td>Up to 14 delayed release capsules or 1 starter pack in 30 days (for taper)</td>
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<td></td>
<td></td>
<td>240 mg</td>
<td>Up to 60 delayed release capsules in 30 days</td>
</tr>
<tr>
<td>Tysabri</td>
<td>300mg/q 4 weeks</td>
<td>See CP</td>
<td>Up to 1 vial per month</td>
</tr>
<tr>
<td>Zinbryta</td>
<td>150mg/month</td>
<td>150 mg/ml</td>
<td>1 syringe per 30 days</td>
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</tbody>
</table>

Multiple Sclerosis agents are NOT covered for members with the following criteria:
- Use not approved by the FDA; AND
- The use is unapproved and not supported by the literature or evidence as an accepted off-label use.

**Medically Necessary** — A service or benefit is Medically Necessary if it is compensable under the MA Program and if it meets any one of the following standards:

- The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.

- The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
The service or benefit will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.

Determination of Medical Necessity for covered care and services, whether made on a Prior Authorization, Concurrent Review, Retrospective Review, or exception basis, must be documented in writing.

The determination is based on medical information provided by the Member, the Member’s family/caretaker and the Primary Care Practitioner, as well as any other Providers, programs, agencies that have evaluated the Member.

All such determinations must be made by qualified and trained Health Care Providers. A Health Care Provider who makes such determinations of Medical Necessity is not considered to be providing a health care service under this Agreement.

References:
24. Ampyra (dalfampridine) [prescribing information]. Ardsley, NY: Acorda Therapeutics Inc; September 2017