MEDICAL POLICY STATEMENT		
Original Effective Date	**Next Annual Review Date**	**Last Review / Revision Date**
10/01/2013	**10/1/2015**	**08/25/2015**
Policy Name		**Policy Number**
Multiple Sclerosis Therapy Class		**SRx-0022**

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) are derived from literature based on and supported by clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any Evidence of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Medical Policy Statement. If there is a conflict between the Medical Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination.

For Medicare plans please reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

A. SUBJECT

Multiple Sclerosis Therapy Class

- **Potassium Channel Blocker**
  - Amypra (dalfampridine)
- **Pyrimidine Synthesis Inhibitor**
  - Aubagio (teriflunomide)
- **Interferon beta-1a**
  - Plegridy
  - Rebif
- **Interferon beta-1b**
  - Avonex
  - Betaseron
  - Extavia
- **Immune Modifier**
  - Copaxone (glatiramer)
- **Sphingosine 1-Phosphate Receptor Modulator**
  - Gilenya (fingolimod)
- **CD52 Binder**
  - Lemtrada (alemtuzumab)
- **Nrf2 Pathway Activator**
  - Tecfidera (dimethyl fumarate)
- **α4-Integrin Binder**
  - Tysabri (natalizumab)

B. BACKGROUND

The CareSource Medication Policies are therapy class policies that are used as a guide when determining health care coverage for our members with benefit plans covering prescription drugs. Medication Policies are written on selected prescription drugs requiring prior authorization or Step-Therapy. The Medication Policy is used as a tool to be interpreted in conjunction with the member's specific benefit plan.

The intent of the Multiple Sclerosis Agents Prior Authorization (PA) Program is to encourage appropriate selection of therapy for patients with remitting relapsing multiple sclerosis based on product labeling, clinical literature and established guidelines as well as to encourage use of preferred agents. The program allows continuation of therapy with a non-preferred MS agent when there is clinical documentation of medical necessity from the treating provider.

Multiple Sclerosis (MS) is an autoimmune inflammatory demyelinating disease involving the central nervous system characterized by various clinical patterns of disease progression and confirmation by MRI results. The most common of these is relapsing-remitting MS (RRMS) characterized by clearly defined relapses associated either with full recovery; or partial recovery and residual deficits. There is typically no progression between disease relapses in RRMS.
A number of immunomodulatory agents have demonstrated beneficial effects in patients with relapsing-remitting multiple sclerosis (RRMS), including a reduced rate of new brain lesions on MRI and a decreased frequency of relapse. As a result patients with a confirmed diagnosis of RRMS should receive disease modifying therapy. On the basis of limited studies supporting concomitant therapy of multiple disease modifying agents (DMA) in MS the criteria will allow coverage of only one DMA at a time.**

Due to the risk of Progressive Multifocal Leukoencephalopathy (PML) with natalizumab therapy, CareSource follows the American Academy of Neurology recommendations that natalizumab be reserved for use in select patients with relapsing remitting disease who have failed other therapies either through continued disease activity, medication intolerance or who have a particularly aggressive initial disease course.

C. DEFINITIONS

- **Ineffective*** is defined as-
  After a 90 day trial:
  a. The patient continues to have clinical relapses while on, Disease Modifying Therapy (two relapses within the past 12 months)
  b. The patient continues to have CNS lesion progression as measured by MRI while on Disease Modifying Therapy
  c. The patient continues to have worsening disability while on Disease Modifying Therapy. Examples of worsening disability include, but are not limited to, decreased mobility timed 25 foot walk (T25FW) or decreased ability to perform activities of daily living due to disease progression

D. POLICY

I. Symptom Management Agents
  A. **Ampyra (dalfampridine)** is a potassium channel blocker indicated to improve walking in patients (18 years and older) with multiple sclerosis (MS)
    1. Ampyra (Dalfampridine) may be considered medically necessary when **ALL** of the following criteria are met:
      1.1 A definitive diagnosis of multiple sclerosis that has been established by a neurologist
      1.2 Prescribed by a neurologist

1.3 The patient has been on a disease modifying agent for at least the last 90 days
1.4 The patient is ambulatory with a baseline timed 25 foot walk (T25FW) between 8 and 45 seconds

II. Disease Modifying Infused Agents
A. **ALL** below agents must meet the following:
1. Definitive diagnosis of a relapsing form of multiple sclerosis (relapsing-remitting or secondary progressing multiple sclerosis) that has been established by a neurologist
2. Prescribed by, or in consultation with, a neurologist or under the guidance of a neurologist
B. **Avonex (Interferon beta-1a), Extavia (Interferon beta-1b) Copaxone 20mg (glatiramer)** may be considered medically necessary when the two (2) above criteria are met
C. **Copaxone 40mg (glatiramer)** may be considered medically necessary with the additional criteria below:
1. Documented compliance issues with Copaxone 20mg in clinical notes
D. **Betaseron (Interferon beta-1b), Plegridy (peg interferon beta-1a) OR Rebif (Interferon beta-1a)** may be considered medically necessary with the additional criteria below:
1. The patient has had a trial of another first line injectable agent (e.g. Extavia, Avonex, or Copaxone), and is documented in clinical notes to be ineffective*, not tolerated or contraindicated
E. **Tysabri (Natalizumab**) may be considered medically necessary with the additional criteria below:
1. Prescriber is registered with the MS TOUCH® Prescribing Program
2. Member has had anti-JCV antibody testing with ELISA prior to initiating treatment and annually thereafter
3. Member has failed other therapies through continued disease activity, medication intolerance or who have a particularly aggressive initial disease course
3.1 The patient has completed a trial with at least one interferon beta product or glatiramer acetate (Copaxone) **and** then Gilenya (fingolimod) and is documented in clinical notes to be ineffective*, or not tolerated or contraindicated.
F. **Lemtrada (alemtuzumab)** may be considered medically necessary when **ALL** of the following criteria are met:
1. The patient has completed a trial with at least one interferon beta product or glatiramer acetate (Copaxone) then Gilenya, and then Tysabri. This is documented in clinical notes to be ineffective*, not tolerated or contraindicated.
2. Patient has had baseline CBC, serum creatinine and thyroid function tests.

III. Disease Modifying Oral Agents
A. **ALL** oral agents must meet the following additional criteria:
1. Patient has had a baseline CBC including lymphocyte count and is not being treated for any infectious diseases
2. The patient has completed a 90 day trial with at least one interferon beta product (Avonex, Rebif, Betaseron, or Extavia) or glatiramer acetate (Copaxone)
B. **Gilenya (fingolimod)** may be considered medically necessary with the additional criteria below:
1. Patient has received baseline electrocardiogram (ECG)
2. The patient does not have any of the following contraindications:
2.1 Prolonged QTc interval ≥ 500 ms

2.2 Use of antineoplastic, immunosuppressive, Class Ia (e.g. disopyramide, procainamide, quinidine) or Class III (e.g. amiodarone, dronedarone, sotalol, dofetilide, ibutilide) antiarrhythmics or immune modulating therapies
2.3 Mobitz Type II second or third-degree AV block without a functioning pacemaker

3. Patient has not had ANY of the following in the last 6 months:
   3.1 Myocardial infarction
   3.2 Unstable angina
   3.3 Stroke
   3.4 TIA
   3.5 Decompensated heart failure requiring hospitalization
4. Patient has had a baseline eye exam

C. **Tecfidera (dimethyl fumarate**) or **Aubagio (teriflunomide)** may be considered medically necessary with the additional criteria below:
   1. The patient has completed a trial with Gilenya and is documented in clinical notes to be ineffective* or not tolerated.

Note: Documented diagnosis must be confirmed by portions of the individual's medical record which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but are not limited to test reports, chart notes from provider's office or hospital admission notes.

ALL other uses of Avonex, Aubagio, Betaseron, Extavia, Copaxone, Ampyra, Gilenya, Rebif, Tecfidera, Tysabri, and Lemtrada and Plegridy are considered experimental/investigational and therefore, will follow CareSource's Off-Label policy.

For Medicare Plan members, reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

If there is no NCD or LCD present, reference the CareSource Policy for coverage.

CONDITIONS OF COVERAGE

HCPCS J1830 Betaseron & Extavia
J2323 Tysabri
J1595 Copaxone
J1826 Avonex
J3490 Plegridy
J3590 Lemtrada
J8499 Gilenya, Tecfidera

CPT

Step Therapy

Under some plans, including plans that use an open or closed formulary, some of the medications in this policy may be subject to step-therapy. Refer to the CareSource formulary tool or PDL for further guidance.

CONDITIONS OF COVERAGE

Office, Outpatient, Home
**Preferred place of service is in the home.
This medication can be self-administered and can be billed through the pharmacy benefit.
Note: CareSource supports administering inject able medications in various setting, as long as those services are furnished in the most appropriate and cost effective setting that are supportive of the patient's medical condition and unique needs and condition. The decision on the most

appropriate setting for administration is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of the specific medication.

AUTHORIZATION PERIOD
Approved initial authorizations are valid for 12 months. Continued treatment may be considered when the member has shown biological response to treatment. A reauthorization after successful initiation period will be placed for 1 year. **ALL** authorizations are subject to continued eligibility.

E. RELATED POLICIES/RULES

F. REVIEW/REVISION HISTORY

Date Issued:	10/01/2013
Date Reviewed:	10/01/2013, 10/16/2014,
Date Revised:	10/16/2014 – Updated ampyra (all forms of MS), added plegridy, updated references, added generic names to the products, and reformatting. 04/07/2015 – Placed in new template, added Copaxone 40, updated definition of relapse, added Gilenya to trial agents for Tysabri 08/25/2015- Add Lemtrada, revised criteria for Tysabri & Gilenya

G. REFERENCES

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13. Rebif [package insert]. Rockland, MA: EMD Serono Inc.; May 2014.
14. Tecfidera [package insert]. Cambridge, MA: Biogen Idec Inc.; April 2015.
15. Tysabri [package insert]. Cambridge, MA: Biogen Idec Inc.; December 2013.
16. Lemtrada [package insert]. Scottsdale, AZ: Sanofi-Genzyme Corporation; Revised April 2015.

This guideline contains custom content that has been modified from the standard care guidelines and has not been reviewed or approved by MCG Health, LLC.

The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.