PHARMACY POLICY STATEMENT

Original Effective Date	Next Annual Review	Last Revision
10/01/2013	10/01/2017	11/21/2016
Policy Name		**Policy Number**
Multiple Sclerosis		SRx-0061
Policy Type		
Medical	Administrative	**PHARMACY** Reimbursement

Pharmacy 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, Pharmacy Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Pharmacy 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 Pharmacy Policy Statement. If there is a conflict between the Pharmacy 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

Contents of Policy

A. INTRODUCTION

Multiple Sclerosis (MS) is a disease of the central nervous stem that involves an immune-mediated process in which the body's immune system abnormally responds against the central nervous system (CNS). When the immune system abnormally responds within the CNS, it attacks myelin and nerve fibers causing damage and formation of scar tissue (sclerosis). When the myelin sheath or nerve fiber is damaged or destroyed, nerve impulses that travel to and from the brain and spinal cord are distorted or interrupted leading to a variety of symptoms. People with MS typically experience one of four disease courses, which can each be classified as mild, moderate or severe. These four disease courses are:

- Clinically Isolated Syndrome (CIS) which is a first episode of neurological symptoms caused by inflammation and demyelination in the CNS
- Relapsing-remitting MS (RRMS), the most common disease course, which is characterized by clearly defined attacks of new or increase neurological symptoms (relapses) followed by periods of partial or complete recovery (remissions)
- Primary progressive MS (PPMS) which is characterized by worsening neurologic function from the onset of symptoms without early relapses and remissions
- Secondary progressive MS (SPMS) which follows an initial relapsing-remitting course which eventually transitions into a course with progressive worsening of neurological function over time

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 Tysabri (natalizumab) therapy, CareSource follows the American Academy of Neurology recommendations that Tysabri 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.

The intent of CareSource Pharmacy Policy Statements is to encourage appropriate selection of patients for therapy according to product labeling, clinical guidelines, and/or clinical studies as well as to encourage use of preferred agents. The CareSource Pharmacy Policy Statement is a guideline for determining health care coverage for our patients with benefit plans covering prescription drugs. Pharmacy Policy Statements are written on selected prescription drugs requiring prior authorization or step therapy. The Pharmacy Policy Statement is used as a tool to be interpreted in conjunction with the member's specific benefit plan.

NOTE: The Introduction section is for your general knowledge and is not to be construed as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals and is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider can also be a place where medical care is given, like a hospital, clinic or lab. This policy informs providers about when a service may be covered.

B. DEFINITIONS

1) Ineffective is defined as one of the below after a 90-day trial:
   a) The member continues to have clinical relapses while on, disease modifying therapy (two relapses within the past 12 months)
   b) The member continues to have CNS lesion progression as measured by MRI while on disease modifying therapy
   c) The member 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

C. POLICY COVERAGE CRITERIA

1. Site of Service

Site of Service Administration	Coverage Criteria
Office, Outpatient, Home	**Preferred place of service is in the home.** **The following medications can be self-administered and can be billed through the pharmacy benefit: Ampyra, Aubagio, Avonex, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Plegridy, Rebif, and Tecfidera.** CareSource supports administering injectable medications in various settings, as long as those services are furnished in the most appropriate and cost effective settings that are supportive of the patient's medical condition(s) and unique needs and condition(s). The decision on the most appropriate setting for administration is based on the member's current medical condition(s) and any required monitoring or additional services that may coincide with the delivery of the specific medication.

2. Coverage Criteria

CareSource will approve the use of the agents listed below and consider its use medically necessary when the criteria have been met for each condition listed below. Prior authorization request should be submitted with chart notes and documentation supporting medical necessity.

- Symptom management medication:
  - Ampyra (dalfampridine)
- Disease Modifying Therapy agents:
  - Injectable agents:
    - Avonex (interferon beta-1a)
    - Betaseron (interferon beta-1b)

- Copaxone (glatiramer acetate)
- Extavia (interferon beta-1b)
- Glatopa (glatiramer actate) 20 mg (generic equivalent of Copaxone)
- Plegridy (peginterferon beta-1a)
- Rebif (interferon beta-1a)
- Zinbryta (declizumab)

- Oral medications:
  - Aubagio (teriflunomide)
  - Gilenya (fingolimod)
  - Tecfidera (dimethyl fumarate)
- Infused medications:
  - Lemtrada (alemtuzumab)
  - Novantrone (mitoxantrone)
  - Tysabri (natalizumab)

Injectable agents:

Condition	Ampyra (dalfampridine) Coverage criteria:
Symptom Management: Walking (Gait) Difficulties	1) Diagnosis of multiple sclerosis confirmed by neurologist. *Include chart notes.* 2) Prescribed by a neurologist. 3) Member is age 18 or older 4) The member has been on a disease modifying agent for at least the last 90 days 5) The member is ambulatory with a baseline timed 25 foot walk (T25FW) between 8 and 45 seconds. *Include chart notes.*

Condition	Avonex, Glatopa 20 mg, Extavia, Rebif Coverage criteria:
Multiple Sclerosis: Relapsing-remitting MS Secondary Progressive MS	1) Diagnosis of a relapsing form of multiple sclerosis (RRMS and SPMS) confirmed by neurologist. *Include chart notes.* 2) Prescribed by, or in consultation with, a neurologist or under the guidance of a neurologist.

Condition	Copaxone 40 mg Coverage criteria:
Multiple Sclerosis: Relapsing-remitting MS Secondary Progressive MS	1) Diagnosis of a relapsing form of multiple sclerosis (RRMS and SPMS) confirmed by neurologist. *Include chart notes.* 2) Prescribed by, or in consultation with, a neurologist or under the guidance of a neurologist. 3) Documented compliance issues with Glatopa 20 mg in clinical notes following at least a 30-day trial. *Include chart notes.*

Condition	Betaseron or Plegridy Coverage criteria:
Multiple Sclerosis: Relapsing-remitting MS Secondary Progressive MS	1) Diagnosis of a relapsing form of multiple sclerosis (RRMS and SPMS) confirmed by neurologist. *Include chart notes.* 2) Prescribed by, or in consultation with, a neurologist or under the guidance of a neurologist. 3) Member has had a trial of another first-line injectable agent (Avonex, Copaxone/Glatopa, Extavia, or Rebif) which was ineffective as defined above, not tolerated, or contraindicated. *Include chart notes.*

Condition	Zinbryta Coverage criteria:
Multiple Sclerosis: Relapsing-remitting MS Secondary Progressive MS	1) Diagnosis of a relapsing form of multiple sclerosis (RRMS and SPMS) confirmed by neurologist. *Include chart notes.* 2) Prescribed by, or in consultation with, a neurologist or under the guidance of a neurologist who is certified with the Zinbryta REMS program. 3) Member is ambulatory (not confined to bed or wheelchair). 4) Member has a negative TB test within the last 6 months. *Include results.* 5) Member has had an inadequate response to two or more disease-modifying drug therapies (Aubagio, Avonex, Betaseron, Copaxone/Glatopa, Extavia, Gilenya, Lemtrada, Plegridy, Rebif, Tecfidera, or Tysabri).

Oral medications:

Condition	Aubagio, Gilenya or Tecfidera Coverage criteria:
Multiple Sclerosis: Relapsing-remitting MS Secondary Progressive MS	1) Diagnosis of a relapsing form of multiple sclerosis (RRMS and SPMS) confirmed by neurologist. *Include chart notes.* 2) Prescribed by, or in consultation with, a neurologist or under the guidance of a neurologist.

Infused medications:

Condition	Lemtrada Coverage criteria:
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	1) Diagnosis of a relapsing form of multiple sclerosis (RRMS and SPMS) confirmed by neurologist. *Include chart notes.* 2) Prescribed by, or in consultation with, a neurologist or under the guidance of a neurologist who is certified with the Lemtrada REMS program. 3) Member has completed a trial with at least one injectable agent (interferon beta product or Copaxone/Glatopa) and then an oral agent (Aubagio, Gilenya, or Tecfidera), and then Tysabri. Trials are noted to be ineffective as defined above, not tolerated, or contraindicated. *Include chart notes.*

Condition	Novantrone Coverage criteria:
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	1) Diagnosis of a relapsing form of multiple sclerosis (RRMS and SPMS) confirmed by neurologist. *Include chart notes.* 2) Prescribed by, or in consultation with, a neurologist or under the guidance of a neurologist. 3) Member has completed a trial with at least one injectable agent (interferon beta product or Copaxone/Glatopa) and then an oral agent (Aubagio, Gilenya, or Tecfidera), and then Tysabri. Trials are noted to be ineffective as defined above, not tolerated, or contraindicated. *Include chart notes.* 4) Left ventricular ejection fraction (LVEF) > 50%

Condition	Tysabri Coverage criteria:
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	1) Diagnosis of a relapsing form of multiple sclerosis (RRMS and SPMS) confirmed by neurologist. *Include chart notes.* 2) Prescribed by, or in consultation with, a neurologist or under the guidance of a neurologist. 3) Member is negative for John Cunningham virus (JCV) with ELISA prior to initiating treatment and annually thereafter. 4) The member has had a trial with at least one of the following medications: Avonex, Betaseron, Copaxone/Glatopa, Extavia, Rebif, Aubagio, Gilenya, or Tecfidera, which was ineffective as

	defined above, not tolerated, or contraindicated. *Include chart notes.*

All other uses of the agents listed above are considered experimental/investigational; and therefore, will follow CareSource's off-label policy.

Please note that this policy is reviewed on an annual basis. New drugs and indications receiving FDA approval may not be reflected in this policy immediately.

Notes:

- Documented diagnosis must be confirmed by portions of the individual's medical record which 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.
- Member is required to have completed the trial(s) listed in the above criteria unless the member is unable to tolerate or has a contraindication to trial medications. Documentation such as chart notes or pharmacy claims may be requested to verify trial(s), intolerance, or contraindication(s).
- Refer to the product package insert for dosing, administration and safety guidelines.
- 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.

3. Dosage and Quantity Limits (listed if applicable)

Information for patients with renal or hepatic impairment is not included. See package insert for individual agents.

Condition	Dosage and Quantity Limit of Ampyra (dalfampridine)
Symptom Management: Walking (Gait) Difficulties	Dosing is 10 mg every 12 hours. Quantity limit of 60 tablets per 30 days.

Condition	Dosage and Quantity Limit of Avonex
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Dosing is 30 mcg once weekly. Quantity limit of 4 vials, syringes, or auto-injector per 30 days.

Condition	Dosage and Quantity Limit of Betaseron and Extavia
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Target dose is 0.25 mg every other day. Quantity limit of 15 subcutaneous kits per 30 days.

Condition	Dosage and Quantity Limit of Copaxone and Glatopa
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Dosing is 20 mg once daily, if using 20 mg dose (preferred with Glatopa). Dosing is 40 mg 3 times per week administered at least 48 hours apart if using 40 mg dose (not available in generic). Quantity limit of up to 30 prefilled syringes per 30 days.

Condition	Dosage and Quantity Limit of Extavia
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Target dose is 0.25 mg every other day. Quantity limit of 15 subcutaneous kits per 30 days.

Condition	Dosage and Quantity Limit of Plegridy
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Maintenance dosing is 125 mcg every 14 days. Quantity limit of 1 Starter Pack for therapy initiation for 28 days. Quantity limit of 2 prefilled syringes or pen-injectors per 28 days for maintenance dosing.

Condition	Dosage and Quantity Limit of Rebif
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Recommended dosing is 22 mcg or 44 mcg 3 times per week. Quantity limit of 1 titration pack per 28 days for therapy initiation. Quantity limit of 12 prefilled syringes or autonjectors per 28 days for maintenance dosing.

Condition	Dosage and Quantity Limit of Zinbryta
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Dosing is 150 mg once monthly. Quantity limit of 1 prefilled syringe per 30 days.

Condition	Dosage and Quantity Limit of Aubagio
Multiple Sclerosis: **Relapsing-remitting MS**	Dosing is 7 or 14 mg once daily.

Secondary Progressive MS	Quantity limit of 30 tablets per 30 days.

Condition	Dosage and Quantity Limit of Gilenya
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Dosing is 0.5 mg daily. Quantity limit of 30 capsules per 30 days.

Condition	Dosage and Quantity Limit of Tecfidera
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Target dosing is 240 mg twice daily. Quantity is limited to 14 of the 120 mg capsules for therapy initiation for first 7 days. Quantity limit of 60 tablets per 30 days for target dosing of 240 mg.

Condition	Dosage and Quantity Limit of Lemtrada
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Dosing is 12 mg daily for 5 consecutive days followed 12 months later by 12 mg daily for 3 consecutive days. Total duration of therapy 24 months. Quantity limit of 60 mg for 12 months initially and reauthorization of 36 mg for 12 months.

Condition	Dosage and Quantity Limit of Novantrone
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Dosing is 12 mg/m^2 every 3 months. Maximum lifetime cumulative dose: 140 mg/m^2.

Condition	Dosage and Quantity Limit of Tysbari
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	Dosing is 300 mg mcg every 4 weeks. Quantity limit of 300 mg every 4 weeks.

4. Authorization Period

Condition	Approval Period
Symptom Management: **Walking (Gait) Difficulties**	The initial authorization Ampyra is valid for 6 months. Continued treatment may be considered with confirmation that the member's walking improved with Ampyra therapy (*include chart notes*). A reauthorization after successful initiation period will be placed for 12 months.

	ALL authorizations are subject to continued eligibility
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	The initial authorization Avonex, Betaseron, Copaxone, Extavia, Plegridy, Rebif, Aubagio, Gilenya, Tecifdera, Lemtrada, and Tysabri is valid for 12 months. Continued treatment may be considered when the member has shown biological response to treatment (*include chart notes*). A reauthorization after successful initiation period will be placed for 12 months for Avonex, Betaseron, Copaxone, Extavia, Plegridy, Rebif, Aubagio, Gilenya, Tecifdera, Lemtrada. Continued treatment may be considered when the member has shown biological response to treatment (*include chart notes*) and is negative for JCV. A reauthorization after successful initiation period will be placed for 12 months for Tysabri. **ALL** authorizations are subject to continued eligibility.
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	The initial authorization Novantrone is valid for 3 months. Continued treatment may be considered when the member has shown biological response to treatment (*include chart notes*) and member has not met maximum lifetime cumulative dose. A reauthorization after successful initiation period will be placed for 3 months. **ALL** authorizations are subject to continued eligibility.
Multiple Sclerosis: **Relapsing-remitting MS** **Secondary Progressive MS**	The initial authorization Zinbryta is valid for 3 months. Continued treatment may be considered when the member meets initial criteria and has shown biological response to treatment (*include chart notes*). A reauthorization after successful initiation period will be placed for 12 months.

	ALL authorizations are subject to continued eligibility

5. Coding

HCPCS	
J1826, Q3025, Q3026, Q3027, Q3028	Avonex
J1830	Betaseron
J1595	Copaxone
J1830	Extavia
J1595	Glatopa
J3490	Plegridy
J1826, J1830, Q3025, Q3026	Rebif
J8499	Aubagio
J8499	Gilenya
J8499	Tecfidera
J3590	Lemtrada
J9293	Novantrone
J2323	Tysabri
J3590	Zinbryta
J3490	Unclassified drugs
J3590	Unclassified biologics

D. RELATED POLICIES

AD-0004: Medical Necessity - Off-Label, Approved Orphan and Compassionate Use Drugs

E. REVIEW/REVISION HISTORY

DATE	ACTION/DESCRIPTION
10/01/2013	Issued, reviewed
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.
10/20/2015	Reviewed. Add definition of 'disease modifying agents' and criteria reference for Tecfidira
10/17/2016	Annual review, updated formatting.

11/26/2016	Updated policy format, references, criteria, and authorization periods. Added Novantrone and Zinbryta.

F. REFERENCES

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12. Tecfidera [package insert]. Cambridge, MA: Biogen Idec Inc.; February 2016.
13. Lemtrada [package insert]. Cambridge, MA: Genzyme Corporation; November 2014.
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18. Goodman AD, Brown TR, Edwards KR, Krupp LB, Schapiro RT, Cohen R, Marinucci LN, Blight AR; MSF204 Investigators. A phase 3 trial of extended release oral dalfampridine in multiple sclerosis. *Ann Neurol.* 2010 Oct; 68(4):494-502.

The Pharmacy Policy detailed above has received due consideration and is approved.