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Subject: Multiple Sclerosis Self Injectable Therapy

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DESCRIPTION:

Multiple sclerosis (MS) is a chronic disease affecting the central nervous system (CNS). It is characterized by triad of inflammation, demyelination, and scarring of the central nervous system and manifests as pathological (immune-mediated CNS demyelination and axonal injury) and clinical (exacerbations, disability progression) dissemination in time and space. Although the clinical course of the disease is capricious, MS has been categorized into four types: clinically isolated syndrome (CIS), relapsing-remitting (RRMS), secondary progressive (SPMS), and primary progressive (PPMS). The most common type is RRMS, which is characterized by acute attacks followed by periods of remission. An initial attack may present as a clinically isolated syndrome (CIS); individuals presenting with this syndrome are high risk for subsequent conversion to clinically definite MS (CDMS) when coupled with MRI lesions consistent with MS.

Although a cure for MS remains elusive, several treatment options slow the progression of the disease and reduce the frequency of relapses. These include dimethyl fumarate (Tecfidera), fingolimod (Gilenya), glatiramer acetate (Copaxone, Glatopa), interferon beta-1a (Avonex, Rebif), interferon beta-1b (Betaseron, Extavia), natalizumab (Tysabri), peg-interferon beta-1a (Plegridy), teriflunomide (Aubagio), alemtuzumab (Lemtrada), and ocrelizumab (Ocrevus).

The exact mechanism by which interferon (IFN) beta therapy exerts its beneficial effects is not clearly delineated; however, multiple clinical studies have demonstrated the ability of IFN beta preparations to reduce the number and severity of relapses and the number of new lesions appearing on magnetic resonance imaging (MRI). IFN beta preparations may also reduce the long-term progression of MS. To date, several head-to-head studies have evaluated differences in the beneficial effects (i.e., clinical, MRI measures of response) between the different types of IFN beta preparations; unfortunately, clinical interpretation of the results is limited by methodologic problems (e.g., short duration, non-blinded design,

non-standardized dosages and/or routes of administration). As such, no consensus has been reached as to whether one preparation should be used in favor over the other.

Glatiramer acetate is also considered a first line option for the treatment of individuals with RRMS. Although glatiramer acetate has not demonstrated efficacy in slowing, reversing, or halting the progression of the disease, it has been proven to delay the time to CDMS among patients who have experienced a first clinical episode and have MRI results consistent with MS. While the efficacy of glatiramer acetate relative to IFN beta therapy has not been established, it may be useful in members who do not respond adequately to or who do not tolerate IFN beta therapy.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

NOTE: Aubagio, Avonex, Betaseron, Glatiramer acetate (by Mylan), Gilenya, Mavenclad, Mayzent, Plegridy, Rebif, and Tecfidera are preferred products for treatment of relapsing forms of multiple sclerosis.

Initiation of Avonex, Rebif, Plegridy or Betaseron **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. The member has a diagnosis of **ONE** of the following forms of multiple sclerosis (MS):
 - a. Relapsing-remitting MS [RRMS]
 - b. Active secondary-progressive MS [SPMS]
 - c. First clinical episode and the member has MRI features consistent with MS
2. The dosage does not exceed FDA approved labeling for the individual agents listed in Table 1.
3. Interferon therapy is **NOT** used in combination with **ANY** of the following:
 - a. Alemtuzumab (Lemtrada)
 - b. Cladribine (Mavenclad)
 - c. Dimethyl fumarate (Tecfidera)
 - d. Fingolimod (Gilenya)
 - e. Glatiramer acetate products (Copaxone, glatiramer acetate, Glatopa)
 - f. Interferon beta-1a (Avonex, Rebif)
 - g. Interferon beta-1b (Betaseron, Extavia)
 - h. Mitoxantrone (Novantrone)
 - i. Natalizumab (Tysabri)
 - j. Ocrelizumab (Ocrevus)
 - k. Peg-interferon beta-1a (Plegridy)
 - l. Siponimod (Mayzent)

m. Teriflunomide (Aubagio)

Approval duration: 1 year

Initiation of Extavia **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. The member has a diagnosis of **ONE** of the following forms of multiple sclerosis (MS)::
 - a. Relapsing-remitting MS [RRMS]
 - b. Active secondary-progressive MS [SPMS]
 - c. First clinical episode and the member has MRI features consistent with MS
2. The member has an inadequate response or contraindication to **ONE** of the following:
 - a. Cladribine (Mavenclad)
 - b. Dimethyl fumarate (Tecfidera)
 - c. Fingolimod (Gilenya)
 - d. Glatiramer acetate
 - e. Interferon beta-1a (Avonex, Rebif)
 - f. Interferon beta-1b (Betaseron)
 - g. Peg-interferon beta-1a (Plegridy)
 - h. Siponimod (Mayzent)
 - i. Teriflunomide (Aubagio)
3. The dosage does not exceed FDA approved labeling for the individual agents listed in Table 1.
4. Interferon therapy is **NOT** used in combination with **ANY** of the following:
 - a. Alemtuzumab (Lemtrada)
 - b. Cladribine (Mavenclad)
 - c. Dimethyl fumarate (Tecfidera)
 - d. Fingolimod (Gilenya)
 - e. Glatiramer acetate products (Copaxone, glatiramer acetate, Glatopa)
 - f. Interferon beta-1a (Avonex, Rebif)
 - g. Interferon beta-1b (Betaseron, Extavia)
 - h. Mitoxantrone (Novantrone)
 - i. Natalizumab (Tysabri)
 - j. Ocrelizumab (Ocrevus)
 - k. Peg-interferon beta-1a (Plegridy)
 - l. Siponimod (Mayzent)
 - m. Teriflunomide (Aubagio)

Approval duration: 1 year

Initiation of glatiramer acetate (by Mylan) **meets the definition of medical necessity** when **ALL** of the following criteria are met

1. The member has a diagnosis of **ONE** of the following forms of multiple sclerosis (MS):
 - a. Relapsing-remitting MS [RRMS]
 - b. Active secondary-progressive MS [SPMS]
 - c. First clinical episode and the member has MRI features consistent with MS
2. The dosage does not exceed FDA-approved labeling listed in Table 1.
3. Glatiramer acetate is **NOT** used in combination with **ANY** of the following
 - a. Alemtuzumab (Lemtrada)
 - b. Cladribine (Mavenclad)
 - c. Dimethyl fumarate (Tecfidera)
 - d. Fingolimod (Gilenya)
 - e. Glatiramer acetate products (Copaxone, Glatopa)
 - f. Interferon beta-1a (Avonex, Rebif)
 - g. Interferon beta-1b (Betaseron, Extavia)
 - h. Mitoxantrone (Novantrone)
 - i. Natalizumab (Tysabri)
 - j. Ocrelizumab (Ocrevus)
 - k. Peg-interferon beta-1a (Plegridy)
 - l. Siponimod (Mayzent)
 - m. Teriflunomide (Aubagio)

Approval duration: 1 year

Initiation of brand Copaxone or Glatopa **meets the definition of medical necessity** when **ALL** of the following criteria are met

1. The member has a diagnosis of **ONE** of the following forms of multiple sclerosis (MS):
 - a. Relapsing-remitting MS [RRMS]
 - b. Active secondary-progressive MS [SPMS]
 - c. First clinical episode and the member has MRI features consistent with MS
2. The member has tried and had intolerable adverse effects to glatiramer acetate (by Mylan) and **ALL** of the following must be submitted:
 - a. The specific intolerance(s) and rationale for using brand Copaxone or Glatopa must be specified
 - b. Completed Medwatch reporting form (FDA 3500) - <https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda>
 - c. Completed Naranjo Adverse Drug reaction probability scale - <https://livertox.nih.gov/Naranjoassessment.pdf>

3. The dosage does not exceed FDA-approved labeling listed in Table 1.
4. Glatiramer acetate is **NOT** used in combination with ANY of the following
 - a. Alemtuzumab (Lemtrada)
 - b. Cladribine (Mavenclad)
 - c. Dimethyl fumarate (Tecfidera)
 - d. Fingolimod (Gilenya)
 - e. Glatiramer acetate products (Copaxone, glatiramer acetate, Glatopa)
 - f. Interferon beta-1a (Avonex, Rebif)
 - g. Interferon beta-1b (Betaseron, Extavia)
 - h. Mitoxantrone (Novantrone)
 - i. Natalizumab (Tysabri)
 - j. Ocrelizumab (Ocrevus)
 - k. Peg-interferon beta-1a (Plegridy)
 - l. Siponimod (Mayzent)
 - m. Teriflunomide (Aubagio)

Approval duration: 1 year

Continuation of interferon beta-1a (Avonex, Rebif), interferon beta-1b (Betaseron, Extavia), peg-interferon beta-1a (Plegridy), or glatiramer acetate (by Mylan) **meets the definition of medical necessity** for the treatment of RRMS, active SPMS, or clinically isolated syndrome when **ALL** of the following criteria are met:

1. Member has demonstrated a beneficial response to the requested agent
2. Authorization/reauthorization for the requested agent has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member currently meets all indication-specific initiation criteria
3. The dose does not exceed FDA-approved labeling as outlined in Table 1
4. Use is **NOT** in combination with any of the following:
 - a. Alemtuzumab (Lemtrada)
 - b. Cladribine (Mavenclad)
 - c. Dimethyl fumarate (Tecfidera)
 - d. Fingolimod (Gilenya)
 - e. Glatiramer acetate products (Copaxone, glatiramer acetate, Glatopa)
 - f. Interferon beta-1a (Avonex, Rebif)
 - g. Interferon beta-1b (Betaseron, Extavia)
 - h. Mitoxantrone (Novantrone)
 - i. Natalizumab (Tysabri)
 - j. Ocrelizumab (Ocrevus)

- k. Peg-interferon beta-1a (Plegridy)
- l. Siponimod (Mayzent)
- m. Teriflunomide (Aubagio)

Approval duration: 1 year

Continuation of brand Copaxone or Glatopa **meets the definition of medical necessity** for the treatment of RRMS, active SPMS, or clinically isolated syndrome when **ALL** of the following criteria are met:

1. The member has tried and had intolerable adverse effects to glatiramer acetate (by Mylan) and ALL of the following must be submitted:
 - a. The specific intolerance(s) and rationale for using brand Copaxone or Glatopa must be specified
 - b. Completed Medwatch reporting form (FDA 3500) - <https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda>
 - c. Completed Naranjo Adverse Drug reaction probability scale - <https://livertox.nih.gov/Naranjoassessment.pdf>
2. Member has demonstrated a beneficial response to the requested agent
3. Authorization/reauthorization for the requested agent has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member currently meets all indication-specific initiation criteria
4. The dose does not exceed FDA-approved labeling as outlined in Table 1
5. Use is NOT in combination with any of the following:
 - a. Alemtuzumab (Lemtrada)
 - b. Cladribine (Mavenclad)
 - c. Dimethyl fumarate (Tecfidera)
 - d. Fingolimod (Gilenya)
 - e. Glatiramer acetate products (Copaxone, glatiramer acetate, Glatopa)
 - f. Interferon beta-1a (Avonex, Rebif)
 - g. Interferon beta-1b (Betaseron, Extavia)
 - h. Mitoxantrone (Novantrone)
 - i. Natalizumab (Tysabri)
 - j. Ocrelizumab (Ocrevus)
 - k. Peg-interferon beta-1a (Plegridy)
 - l. Siponimod (Mayzent)
 - m. Teriflunomide (Aubagio)

Approval duration: 1 year

Glatiramer acetate (by Mylan) **meets the definition of medical necessity** when used as a single agent for the following designated Orphan Drug indication when the maximum FDA-approved dose is not exceeded:

1. Treatment of amyotrophic lateral sclerosis (ALS)

Approval Duration: 1 year

Table 1: Maximum Dosage Limits†

Drug	Maximum Dose
Avonex (IFN beta-1a)	30 mcg IM weekly
Rebif (IFN beta-1a)	44 mcg SQ 3 times a week
Betaseron (IFN beta-1b)	0.3 mg SQ every other day
Extavia (IFN beta-1b)	0.3 mg SQ every other day
Plegridy (peg-interferon beta-1a)	125 mcg every 14 days
Copaxone 20 mg (glatiramer acetate)	20 mg SQ daily
Copaxone 40 mg (glatiramer acetate)	40 mg SQ 3 times a week
glatiramer acetate 20 mg (by Mylan)	20 mg SQ daily
glatiramer acetate 40 mg (by Mylan)	40 mg SQ 3 times a week
Glatopa 20 mg (glatiramer acetate)	20 mg SQ daily
Glatopa 40 mg (glatiramer acetate)	40 mg SQ 3 times a week

†Based on FDA-approved labeling
IFN=Interferon; IM=Intramuscularly; SQ=Subcutaneously

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

Table 2: FDA-Approved Indications and Recommended Dosing

Drug	FDA-approved indication	Usual Dosage	Comments
Avonex (IFN beta-1a)	Relapsing forms of MS†	30 mcg IM once a week	If a dose is missed, it should be given as soon as possible; do not give 2 injections within 2 days of each other
Rebif (IFN beta-1a)	Relapsing forms of MS†	22 or 44 mcg SQ three times weekly	Each dose should be given at least 48 hours apart. Refer to the package insert for titration schedule.
Plegridy (pegIFN beta-1a)	Relapsing forms of MS†	125 mcg every 14 days	For SQ injection only
Betaseron (IFN beta-1b)	Relapsing forms of MS†	0.25 mg SQ every other day	Refer to the package insert for titration schedule.
Extavia (IFN beta-1b)	Relapsing forms of MS†	0.25 mg SQ every other day	

Copaxone (glatiramer acetate)	Relapsing forms of MS†	20 mg SQ daily or 40 mg SQ three times a week	For SQ injection only; allows solution to warm to room temperature.
glatiramer acetate (by Mylan)	Relapsing forms of MS†	20 mg SQ daily or 40 mg SQ three times a week	For SQ injection only; allows solution to warm to room temperature.
Glatopa (glatiramer acetate)	Relapsing forms of MS†	20 mg SQ daily or 40 mg SQ three times a week	For SQ injection only; allows solution to warm to room temperature.
†Includes clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease in adults. IFN=Interferon; IM=Intramuscularly; SQ=Subcutaneously			

Table 3: Recommended Dosage Adjustments†

Avonex (IFN beta-1a)	No dosage adjustments are recommended for either hepatic or renal impairment
Rebif (IFN beta-1a)	Leukopenia and abnormal liver function tests may require a reduction in dose (see “Precautions/Warnings”). No dosage adjustments are recommended for renal impairment.
Plegridy (PegIFN beta-1a)	Dose should be titrated: 63 mcg on day 1, 94 mcg on day 15, and 125 mcg on day 29.
Betaseron (IFN beta-1b)	No dosage adjustments are recommended for either hepatic or renal impairment
Extavia (IFN beta-1b)	
Copaxone (glatiramer acetate)	
Glatiramer acetate (by Mylan)	
Glatopa (glatiramer acetate)	
†Interferon beta and glatiramer pharmacokinetics have not been determined in patients with hepatic or renal impairment; IFN=Interferon	

Table 4: Drug Availability

Avonex (IFN beta-1a)	<ul style="list-style-type: none"> • 30 mcg powder for injection (single-use vial) • 30 mcg/0.5 mL prefilled syringe • 30 mcg/0.5 mL auto-injector for injection
Rebif (IFN beta-1a)	<ul style="list-style-type: none"> • 22 mcg/0.5 mL prefilled syringe • 44 mcg/0.5 mL prefilled syringe • Titration pack (contains six 22 mcg/0.5 mL and six 8.8 mcg/0.2 mL prefilled syringes)
Plegridy (PegIFN beta-1a)	<ul style="list-style-type: none"> • 125 mcg/0.5 mL prefilled syringe • 125 mcg/0.5 mL prefilled syringe • Starter pack: 63 mcg/0.5 mL prefilled pen, 0.94 mcg/0.5 mL prefilled pen, 125 mcg/0.5 mL prefilled pin • Starter pack: 63 mcg/0.5 mL prefilled syringe, 0.94 mcg/0.5 mL prefilled syringe, 125 mcg/0.5 mL prefilled syringe
Betaseron (IFN beta-1b)	0.3 mg powder for injection kit (contains a single-use vial and a prefilled

	single-use syringe containing 1.2 mL of diluent)
Extavia (IFN beta-1b)	0.3 mg powder for injection kit (contains a single-use vial and a prefilled single-use syringe containing 1.2 mL of diluent)
Copaxone (glatiramer acetate)	20 mg/mL or 40 mg/mL prefilled syringe
glatiramer acetate (by Mylan)	20 mg/mL or 40 mg/mL prefilled syringe
Glatopa (glatiramer acetate)	20 mg/mL or 40 mg/mL prefilled syringe
IFN=Interferon	

CONTRAINDICATIONS:

Interferon beta: contraindicated in persons with a history of hypersensitivity to interferon beta or albumin (human)

Glatiramer acetate: contraindicated in persons with a history of hypersensitivity to mannitol

PRECAUTIONS/WARNINGS:

Interferon beta (Avonex, Rebif, Betaseron, Extavia):

Hepatic injury: monitor liver function tests. Consider discontinuation if hepatic injury occurs.

Depression, suicide, and psychotic disorders: Monitor and report any symptoms. Consider discontinuation if depression occurs. Use with caution in persons with depression.

Injection site necrosis: Typically, injection site necrosis occurs within the first 4 months of therapy; however, post-marketing reports of injection site necrosis occurring over 1 year after initiation of therapy have been received. Necrosis may occur at single or multiple injection sites. Injection sites should be rotated on a regular basis.

Anaphylaxis: Rare but significant allergic reactions can occur following interferon beta therapy.

Autoimmune disorders: There have been post-marketing reports of autoimmune disorders of multiple target organs, including idiopathic thrombocytopenia and hyper- and hypothyroidism. Rare cases of autoimmune hepatitis have also been reported. Monitor patients for signs of these disorders and consider discontinuation.

Seizures: Use with caution in patients with preexisting seizure disorders. A relationship between occurrence of seizures and the use of Avonex® has not been established.

Decreased peripheral blood counts: monitor complete blood counts.

Thrombotic microangiopathy (TMA): cases have been reported. Discontinue if TMA occurs.

Congestive heart failure: monitor with preexisting cardiac disease or worsening cardiac symptoms.

Children: The safety and efficacy of glatiramer have not been established in persons younger than 18 years of age.

Pregnancy and Nursing:

- All interferon beta preparations are Pregnancy Category C; there are no adequate and well-controlled studies of interferon beta preparations in pregnant women.

- Additionally, no human studies have investigated the effects of interferon beta in breast-fed infants. According to the manufacturers of Betaseron and Extavia, these agents should be avoided in breast feeding. The manufacturers of Avonex and Rebif recommend cautious use of either product in nursing women.

Glatiramer acetate products (Copaxone, glatiramer acetate, Glatopa)

Immediate post-injection reaction: a constellation of symptoms immediately after injection that includes at least 2 of the following: anxiety, chest pain, constriction of the throat, dyspnea, flushing, palpitations, and urticaria. In general, it is transient and self-limiting and occurs after the first few months of treatment. This reaction may occur more than once in a given member.

Chest pain: Transient chest pain - without any long-term effects - may occur one or more times, either as part of the post-injection reaction or separately. While some of these episodes occurred in the context of the immediate post-injection reaction previously described, many did not.

Lipoatrophy and skin necrosis: Localized lipoatrophy and, rarely, injection site skin necrosis at injection sites have been reported during post-marketing experience. Careful rotation of injection sites is recommended so no single area is used for injections more than one time per week.

Immunosuppression: Because glatiramer can modify immune response, it may interfere with immune functions. For example, treatment with glatiramer may interfere with the recognition of foreign antigens in a way that would undermine the body's tumor surveillance and its defenses against infection.

Children: The safety and efficacy of glatiramer have not been established in patients younger than 18 years of age.

Pregnancy and Nursing:

- Pregnancy Category B: There are no adequate and well-controlled studies of glatiramer acetate in pregnant women; however, administration of glatiramer acetate to pregnant rats and rabbits resulted in no adverse effects on fetal development at doses up to 37.5 mg/kg/day (18 and 36 time, respectively, the therapeutic human dose of 20 mg/day on a mg/m2 basis).
- No human studies have investigated the effects of glatiramer acetate on breast-fed infants and caution in nursing women is recommended.

BILLING/CODING INFORMATION:

HCPCS Coding:

C9399	Unclassified drugs or biologicals (Plegridy)
J1595	Injection, glatiramer acetate, 20 mg (Copaxone, Glatopa)
J1826	Injection, interferon beta-1a, 30 mcg (Avonex)
J1830	Injection, interferon beta-1b, 0.25 mg (Betaseron, Extavia)
J3590	Unclassified biologic (Plegridy)
Q3027	Injection, interferon beta-1a, 1 mcg for subcutaneous use (Avonex)
Q3028	Injection, interferon beta-1a, 1 mcg for subcutaneous use (Rebif)

ICD-10 Diagnosis Codes That Support Medical Necessity:

G35	Multiple sclerosis
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REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

DEFINITIONS:

Clinically isolated syndrome (CIS): the first clinical presentation of disease that shows characteristics of inflammatory demyelination that could be MS but has yet to fulfill criteria of dissemination in time.

Primary-progressive multiple sclerosis (PPMS): Steadily progressive course from onset; occurs in 10-15% of patients with MS.

Relapsing-remitting multiple sclerosis (RRMS): Characterized by acute attacks followed by periods of remission; primary form of MS that occurs in approximately 85% of patients.

Secondary-progressive multiple sclerosis (SPMS): An initial period of RRMS, followed by a steadily progressive course, with acute relapses (active disease) or without acute relapses (not active disease); 75-85% of patients diagnosed with RRMS will transition to SPMS

RELATED GUIDELINES:

[Botulinum Toxins, 09-J0000-29](#)

[Cladribine \(Mavenclad\), 09-J3000-34](#)

[Deep Brain Stimulation, 02-61000-24](#)

[Evoked Potentials, Intraoperative Neurophysiologic Testing, and Quantitative Electroencephalography \(QEEG\), 01-95805-13](#)

[Functional Neuromuscular Stimulation, 09-E0000-54](#)

[Immune Globulin Therapy, 09-J0000-06](#)

[Magnetic Resonance Imaging \(MRI\) Brain and Head, 04-70540-11](#)

[Natalizumab \(Tysabri®\) IV, 09-J0000-73](#)

[Ocrelizumab \(Ocrevus\), 09-J2000-78](#)

[Siponimod \(Mayzent\), 09-J3000-35](#)

[Wheelchairs and Wheelchair Accessories, 09-E0000-35](#)

OTHER:

None

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the BCBSF Pharmacy Policy Committee on 10/09/19.

GUIDELINE UPDATE INFORMATION:

10/15/11	New Pharmacy Coverage Guideline.
10/15/12	Review and revision to guideline; consisting of revising description and position statement, updating dosage/administration, precautions/warnings, billing codes, definition, and references, and added contraindication section.

01/15/13	Revision to guideline; consisting of modifying position statement to disallow concurrent use of other MS agents.
04/15/13	Review and revision to guideline; consisting of revising position statement to include continuation criteria.
10/15/13	Review and revision to guideline; consisting of revising position statement to include orphan drug indications and approval duration; updating references and related guidelines.
01/01/14	Revision to guideline; consisting of updating position statement
03/15/14	Revision to guideline; consisting of updating position statement and other sections with newly approved dosing for glatiramer.
10/15/14	Review and revision to guideline; consisting of updating references.
01/01/15	Revision to guideline; consisting of updating position statement.
04/15/15	Revision to guideline; consisting of updating quantity limits for betaseron and extavia.
10/15/15	Review and revision to guideline; consisting of updating position statement, dosage/administration, coding, references.
11/01/15	Revision: ICD-9 Codes deleted.
01/01/17	Review and revision to guideline; consisting of updating position statement, dosage/administration, precautions, coding, and references.
10/15/17	Review and revision to guideline; consisting of updating position statement and references.
05/15/18	Revision to guideline; consisting of removal of daclizumab (product no longer available).
12/15/18	Review and revision to guideline; consisting of updating position statement and references.
04/01/19	Review and revision to guideline; consisting of updating position statement and references.
07/15/19	Review and revision to guideline; consisting of updating position statement and references.
11/15/19	Review and revision to guideline; consisting of updating position statement, description and references.