09-J1000-30

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Subject: Brand Gilenya™ Capsule and Tascenso ODT™

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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.

Fingolimod is an immunomodulatory agent that is used to reduce the frequency of relapses and delay the accumulation of physical disability in patients with RRMS. Fingolimod has a novel mechanism of action and exerts its physiologic effects through attachment to the sphingosine-1 phosphate receptor, which is plays a role in immune function regulation. Fingolimod capsule (Gilenya) is Food and Drug administration (FDA) approved for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients 10 years of age and older. A fingolomod oral disentigrating tablet (Tascenso ODT) is FDA approved for the treatment of relapsing forms of MS in pediatric patients 10 years of age and older.

In 2018, the American Academy of Neurology published a practice guideline on the use of disease-modifying therapy for adults with multiple sclerosis which includes an assessment of the effectiveness and safety of fingolimod in the treatment of MS. Fingolimod has demonstrated a reduction in measures

of disease activity including clinical relapse rate, new and enlarging T2 lesions, and disability progression in patients with relapsing MS. Fingolimod has also shown a reduction in relapses and MRI measures in a sub-group analysis in patients with relapsing MS with highly active disease.

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: Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, and Zeposia are the preferred brand products for treatment of relapsing forms of multiple sclerosis. The preferred generic products include dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan), and teriflunomide (generic). Dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan, Glatopa), and teriflunomide (generic) do not require prior authorization.

Initiation of brand Gilenya™ **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. The member is diagnosed with **ONE** of the following forms of multiple sclerosis (MS):
    a. Relapsing remitting multiple sclerosis [RRMS]
    b. Active secondary progressive MS [SPMS]
    c. First clinical episode and member has MRI features consistent with MS
2. **BOTH** of the following (a and b):
    a. The member has tried and had intolerable adverse effects to generic fingolimod and **ALL** of the following must be submitted:
        i. The specific intolerance(s) and rationale for using brand Gilenya must be specified
        ii. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda
        iii. Completed Naranjo Adverse Drug reaction probability scale - https://assets.guidewell.com/m/2736e82ff52fe22d/original/mcg-naranjo-algorithm.pdf
    b. **ONE** of the following (i, ii, or iii) – documentation must be submitted:
        i. The patient has highly active MS disease activity and **BOTH** of the following:
            1. The patient has ≥ 2 relapses in the previous year

2. **ONE** of the following:
    a. The patient has ≥ 1 gadolinium enhancing lesion on MRI
    b. The patient has significant increase in T2 lesion load compared with a previous MRI

ii. The patient has been treated with at least 3 MS agents from different drug classes

iii. **ONE** of the following (1, 2, or 3):
    1. The patient has tried and had an inadequate response to ONE preferred brand agent (Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, Zeposia)
    2. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to **ONE** preferred brand agent (Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, Zeposia)
    3. The patient has a FDA labeled contraindication to ALL preferred brand agents (Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, Zeposia)

3. Fingolimod will not be used in combination with **ANY** of the following:
    a. Alemtuzumab (Lemtrada)
    b. Cladribine (Mavenclad)
    c. Dimethyl fumarate (Tecfidera)
    d. Diroximel fumarate (Vumerity)
    e. Glatiramer acetate (Copaxone, Glatopa)
    f. Interferon beta-1a (Avonex, Rebif)
    g. Interferon beta-1b (Betaseron, Extavia)
    h. Mitoxantrone (Novantrone)
    i. Monomethyl fumarate (Bafiertam)
    j. Natalizumab (Tysabri)
    k. Ocrelizumab (Ocrevus)
    l. Ofatumumab (Kesimpta)
    m. Ozanimod (Zeposia)
    n. Peg-interferon beta-1a (Plegridy)
    o. Ponesimod (Ponvory)
    p. Rituximab (Rituxan or biosimilars)

q. Siponimod (Mayzent)

r. Teriflunomide (Aubagio)

s. Ublituximab (Briumvi)

4. The member does not have any of the following:

    a. History (within the last 6 months) of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or NYHA Class III/IV heart failure

    b. History or presence of Mobitz Type II second- or third-degree AV block or sick sinus syndrome (unless member has a functioning pacemaker)

    c. Prolonged QT interval (i.e., QTc > 500 ms)

    d. Concomitant therapy with a Class Ia (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol, dofetilide) anti-arrhythmic drug

5. The dosage does not exceed **ONE** of the following:

    a. 0.25 mg daily for a member 40 kg or less

    b. 0.5 mg daily using the fewest capsules per day for a member more than 40 kg

Approval duration: 1 year

Continuation of brand Gilenya™ **meets the definition of medical necessity when ALL** of the following criteria are met:

1. Member has demonstrated a beneficial response to therapy for treatment of RRMS, active SPMS, or clinically isolated syndrome
2. Authorization/reauthorization for fingolimod has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member previously met all indication-specific initiation criteria
3. The member has tried and had intolerable adverse effects to generic fingolimod and ALL of the following must be submitted:

    a. The specific intolerance(s) and rationale for using brand Gilenya 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://assets.guidewell.com/m/2736e82ff52fe22d/original/mcg-naranjo-algorithm.pdf

4. Fingolimod will not be in combination with **ANY** of the following:

    a. Alemtuzumab (Lemtrada)

    b. Cladribine (Mavenclad)

c. Dimethyl fumarate (Tecfidera)
d. Diroximel fumarate (Vumerity)
e. Glatiramer acetate (Copaxone, Glatopa)
f. Interferon beta-1a (Avonex, Rebif)
g. Interferon beta-1b (Betaseron, Extavia)
h. Mitoxantrone (Novantrone)
i. Monomethyl fumarate (Bafiertam)
j. Natalizumab (Tysabri)
k. Ocrelizumab (Ocrevus)
l. Ofatumumab (Kesimpta)
m. Ozanimod (Zeposia)
n. Peg-interferon beta-1a (Plegridy)
o. Ponesimod (Ponvory)
p. Rituximab (Rituxan or biosimilars)
q. Siponimod (Mayzent)
r. Teriflunomide (Aubagio)
s. Ublituximab (Briumvi)

5. The dose does not exceed **ONE** of the following:
    a. 0.25 mg daily for a member 40 kg or less
    b. 0.5 mg daily using the fewest capsules per day for a member more than 40 kg

Approval duration: 1 year

Initiation of fingolimod tablets (Tascenso ODT) **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. **ONE** of the following (a or b) – documentation must be submitted:
    a. The member is 18 year of age or older and **BOTH** of the following (i and ii):
        i. The member has tried and had intolerable adverse effects to generic fingolimod and **ALL** of the following must be submitted:
            1. The specific intolerance(s) and rationale for using Tascenso ODT must be specified

2. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda
3. Completed Naranjo Adverse Drug reaction probability scale - https://assets.guidewell.com/m/2736e82ff52fe22d/original/mcg-naranjo-algorithm.pdf

ii. **ONE** of the following (1, 2, or 3):

1. The patient has highly active MS disease activity and **BOTH** of the following:
    a. The patient has ≥ 2 relapses in the previous year
    b. **ONE** of the following:
        i. The patient has ≥ 1 gadolinium enhancing lesion on MRI
        ii. The patient has significant increase in T2 lesion load compared with a previous MRI
2. The patient has been treated with at least 3 MS agents from different drug classes
3. **ONE** of the following (a,b,or c):
    a. The patient has tried and had an inadequate response to **ONE** preferred brand agent (Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, Zeposia)
    b. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to **ONE** preferred brand agent (Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, Zeposia)
    c. The patient has a FDA labeled contraindication to ALL preferred brand agents (Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, Zeposia)

b. The member is 17 years of age or younger and **ONE** of the following (1, 2, or 3):

1. The patient has highly active MS disease activity and **BOTH** of the following:
    a. The patient has ≥ 2 relapses in the previous year
    b. **ONE** of the following:
        i. The patient has ≥ 1 gadolinium enhancing lesion on MRI
        ii. The patient has significant increase in T2 lesion load compared with a previous MRI
2. The patient has been treated with at least 3 MS agents from different drug classes

3. **ONE** of the following (a,b, c, or d):
    a. The request is for Tascenso ODT 0.25 mg for a member 40 kg or less
    b. The patient has tried and had an inadequate response to dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan, Glatopa), **OR** teriflunomide (generic)
    c. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan, Glatopa), **OR** teriflunomide (generic)
    d. The patient has a FDA labeled contraindication to both dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan, Glatopa), **AND** teriflunomide (generic)

3. Fingolimod is **NOT** used in combination with ANY of the following:
    a. Alemtuzumab (Lemtrada)
    b. Cladribine (Mavenclad)
    c. Dimethyl fumarate (Tecfidera)
    d. Diroximel fumarate (Vumerity)
    e. Fingolimod (Gilenya)
    f. Glatiramer acetate products (Copaxone, glatiramer acetate, Glatopa)
    g. Interferon beta-1a (Avonex, Rebif)
    h. Interferon beta-1b (Betaseron, Extavia)
    i. Mitoxantrone (Novantrone)
    j. Monomethyl fumarate (Bafiertam)
    k. Natalizumab (Tysabri)
    l. Ocrelizumab (Ocrevus)
    m. Ofatumumab (Kesimpta)
    n. Ozanimod (Zeposia)
    o. Peg-interferon beta-1a (Plegridy)
    p. Ponesimod (Ponvory)
    q. Rituximab (Rituxan or biosimilars)
    r. Siponimod (Mayzent)
    s. Teriflunomide (Aubagio)
    t. Ublituximab (Briumvi)
4. The member does not have any of the following:

a. History (within the last 6 months) of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or NYHA Class III/IV heart failure

b. History or presence of Mobitz Type II second- or third-degree AV block or sick sinus syndrome (unless member has a functioning pacemaker)

c. Prolonged QT interval (i.e., QTc > 500 ms)

d. Concomitant therapy with a Class Ia (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol, dofetilide) anti-arrhythmic drug

5. The dose does not exceed **ONE** of the following:

    a. 0.25 mg daily for a member 40 kg or less

    b. 0.5 mg daily using the fewest tablets per day for a member more than 40 kg

Approval duration: 1 year

Continuation of fingolimod tablets (Tascenso ODT) **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 previously met all indication-specific initiation criteria
3. Use is **NOT** in combination with any of the following:
    a. Alemtuzumab (Lemtrada)
    b. Cladribine (Mavenclad)
    c. Dimethyl fumarate (Tecfidera)
    d. Diroximel fumarate (Vumerity)
    e. Fingolimod (Gilenya)
    f. Glatiramer acetate products (Copaxone, glatiramer acetate, Glatopa)
    g. Interferon beta-1a (Avonex, Rebif)
    h. Interferon beta-1b (Betaseron, Extavia)
    i. Mitoxantrone (Novantrone)
    j. Monomethyl fumarate (Bafiertam)
    k. Natalizumab (Tysabri)
    l. Ocrelizumab (Ocrevus)
    m. Ofatumumab (Kesimpta)
    n. Ozanimod (Zeposia)

o. Peg-interferon beta-1a (Plegridy)

p. Ponesimod (Ponvory)

q. Rituximab (Rituxan or biosimilars)

r. Siponimod (Mayzent)

s. Teriflunomide (Aubagio)

t. Ublituximab (Briumvi)

4. The dose does not exceed **ONE** of the following:

    1. 0.25 mg daily for a member 40 kg or less

    2. 0.5 mg daily using the fewest tablets per day for a member more than 40 kg

Approval duration: 1 year

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.

FDA-Approved: Fingolimod capsule (Gilenya) is approved for the treatment of relapsing forms of multiple sclerosis to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients 10 years of age and older. Fingolimod should be administered as 0.5 mg oral capsule once daily in adults and pediatric patients 10 years of age and older weighing more than 40 kg, with or without food. For patients less than or equal to 40 kg and 10 years of age and older, administer 0.25 mg oral capsule once-daily, with or without food. Fingolimod orally disentigrating tablet (Tascenso ODT) is approved for the treatment of relapsing forms of multiple sclerosis to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients 10 years of age and older. For patients who weigh less than or equal to 40 kg, the dose is a 0.25 mg daily. For patients greater than 40 kg, the dose is 0.5 mg daily. The tablet should be taken with or without food. The tablet is placed directly on the tongue and should be allowed to dissolve before swallowing.

First Dose Monitoring:

- The first dose of fingolimod should be administered in a setting that has adequate resources to manage symptomatic bradycardia that occurs following initiation of treatment. The heart rate typically decreases within an hour and the Day 1 nadir generally occurs within approximately 6 hours. The nadir can be observed up to 24 hours following the first dose in some patients. Hourly pulse and blood pressure should be performed
- An ECG should be obtained prior to initiation and at end of observation period
- Monitor symptomatic bradycardia with ECG until resolved. Continue overnight and repeat first-dose monitoring.

- Observe patients overnight if at higher risk of symptomatic bradycardia, heart block, prolonged QTc interval, or if taking drugs with known risk of torsades de pointes.
- Additional observation should be performed if at the end of the 6-hour period if any of the following occurs:
    - If the heart rate is less than 45 beats per minute in adults, less than 55 bpm in patients aged 12 years and above, or less than 60 bpm in pediatric patients aged 10 to below 12 years
    - If the heart rate is at the lowest value at the end of the observation period;
    - If the ECG shows new onset second degree or higher AV block

Re-initiation of Therapy Following Discontinuation:

- If fingolimod therapy is discontinued for more than 14 days, after the first month of the treatment, the effects on heart rate and AV conduction may recur on reintroduction and the same precautions (first dose monitoring) should apply.
- Within the first two weeks of treatment, first dose procedures are recommended after interruption of one day or more
- Within the first three or four weeks of treatment, first dose procedures are recommended after treatment interruption of more than 7 days.

Recommended Dose Adjustments:

- Hepatic Impairment
    - Dosage adjustments are not indicated for members with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment
    - Fingolimod exposure is doubled in members with severe (Child-Pugh Class C) hepatic impairment; as such, fingolimod should be used cautiously in members with severe hepatic impairment. Additionally, close monitoring should be performed because the risk of adverse reactions may be greater.
- Renal Impairment: The serum concentration of some fingolimod metabolites was increased (up to 13-fold) in individuals with renal impairment. The toxicity of these metabolites has not been fully explored and the serum concentration of these metabolites has not been assessed in patients with mild or moderate renal insufficiency.
- Special Populations: The safety and efficacy of fingolimod has not been adequately evaluated in patients over the age of 65. Fingolimod should be used with caution in this population considering the higher frequency of hepatic and renal impairment. The safety and efficacy of fingolimod has not been evaluated in individuals less than 18 years of age.

Missed Dose: recommendations for missed doses are not included in the manufacturer's labeling; see "Re-initiation of therapy following discontinuation" above for the appropriate course of action if therapy is initiated following discontinuation or if therapy is interrupted for one day or more.

Drug Availability: Fingolimod (Gilenya) is supplied as a 0.25 mg and 0.5 mg capsule. Fingolimod (Tascenso ODT) is supplied as a 0.25 mg and 0.5 mg tablet.

PRECAUTIONS:

Contraindications

Fingolimod therapy is contraindicated in the following members:

- Members with a history (within the last 6 months) of myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure with hospitalization or Class III/IV heart failure
- Members with a history or presence of Mobitz Type II second- or third-degree AV block or sick sinus syndrome, unless member has a functioning pacemaker
- Members with a baseline QTc interval of ≥ 500 ms
- Members prescribed concomitant Class Ia or Class III anti-arrhythmic therapy
- Members with hypersensitivity to fingolimod or its excipients

Warnings/Precautions

Bradycardia and AV Block: decreases in heart rate and/or AV conduction can occur following fingolimod initiation; members should be closely monitored (see "Dosage and Administration" for additional information).

Infection: fingolimod therapy my increase the risk of infection. A recent complete blood count (CBC) should be available prior to fingolimod initiation. Members should be monitored for signs and symptoms of infection during treatment and for two months after discontinuation. Fingolimod should not be initiated in members with active acute or chronic infections. All members receiving fingolimod should receive the varicella vaccine, or have evidence of antibodies to varicella zoster virus.

Progressive multifocal leukoencephalopathy (PML): withhold at the first sign or symptom suggestive of PML. Immune reconstitution inflammatory syndrome (IRIS) has been reported in patients treated with fingolimod who developed PML and subsequently discontinued treatment. IRIS presents as a clinical decline in the patient's condition that may be rapid, can lead to serious neurological complications or death, and is often associated with characteristic changes on MRI. Monitor for development of IRIS.

Macular edema: macular edema can occur with or without visual symptoms. An ophthalmologic evaluation should be performed before and re-evaluated at 3-4 months following fingolimod initiation. Visual acuity should be monitored at baseline and during routine evaluation of members. Members with diabetes mellitus or a history of uveitis are at an increased risk for macular edema and should have regular ophthalmologic evaluation

Malignancies: suspicious skin lesions should be evaluated. An increase in the incidence of cutaneous malignancies including basal cell carcinoma (BCC) and melanoma occurred in clinical trials as compared to placebo. Cases of lymphoma have also occurred including T-cell, B-cell, and CNS lymphoma.

Posterior reversible encephalopathy syndrome (PRES): Rare cases of PRES have occurred. Symptoms may include sudden onset of severe headache, altered mental status, visual disturbances, and seizure. If suspected discontinue.

Respiratory effects: fingolimod therapy has been associated with a decrease in pulmonary function tests. Spirometry and diffusion lung capacity for carbon monoxide should be obtained when clinically indicated.

Hepatic effects: fingolimod therapy has been associated with increases in liver transaminases. Liver function tests (LFTs) should be obtained prior to fingolimod initiation and assessed if hepatic injury is suspected. If significant liver injury occurs, fingolimod should be discontinued.

Pregnancy and Nursing:

- There are no adequate and well-controlled studies in pregnant women; however, in oral studies conducted in rates and rabbits, fingolimod demonstrated developmental toxicity, including teratogenicity. Female members of childbearing potential should be advised to use effective contraception during treatment and 2 months after stopping fingolimod.
- A pregnancy registry has been established to collect information about the effect of fingolimod use during pregnancy. Healthcare providers are encouraged to enroll pregnant patients, or pregnant members may register themselves in the fingolimod pregnancy registry by calling 1-877-598-7237 or visiting www.gilenyapregnancyregistry.com
- Fingolimod is excreted into the milk of lactating rats and excretion into human milk is probable. No human studies have investigated the effects of fingolimod on breast-fed infants and the risk and benefit of breastfeeding and treatment with fingolimod should be considered.

Increased blood pressure: monitor during treatment. Increases in blood pressure occurred in clinical trials as compared to placebo.

Immune system effects following discontinuation: Fingolimod remains in the blood for up to 2 months following the last dose. Lymphocyte counts may be affected during this time and precaution is advised with initiation of other drugs during this time.

Hypersensitivity reactions: Reactions including rash, urticaria, and angioedema have been reported.

BILLING/CODING INFORMATION:

HCPCS Coding:

J8499	Prescription drug, oral, nonchemotherapeutic, NOS

ICD-10 Diagnosis Codes That Support Medical Necessity:

G35	Multiple sclerosis

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.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

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:

Alemtuzumab (Lemtrada), 09-J2000-27

Cladribine (Mavenclad), 09-J3000-34

Dimethyl Fumarate (Tecfidera), Diroximel fumarate (Vumerity), and Monomethyl fumarate (Bafiertam), 09-J1000-96

Multiple Sclerosis Self Injectable Therapy, 09-J1000-39

Natalizumab (Tysabri®) IV, 09-J0000-73

Ocrelizumab (Ocrevus), 09-J2000-78

Ofatumumab (Kesimpta), 09-J3000-84

Ozanimod (Zeposia), 09-J3000-70

Siponimod (Mayzent), 09-J3000-35

Teriflunomide (Aubagio), 09-J1000-82

OTHER:

None applicable.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 10/11/23.

GUIDELINE UPDATE INFORMATION:

01/01/11	New Medical Coverage Guideline.
06/15/11	Review and revision to guideline; consisting of updating references.
06/15/12	Review and revision to guideline; consisting of updating description, position statement, precautions, coding and references.
10/15/12	Review and revision to guideline; consisting of revising position statement and description section, updating precautions/warnings, definition, and reference sections, adding contraindications section.
10/15/13	Review and revision to guideline; consisting of revising position statement updating references.
01/01/14	Revision to guideline; consisting of updating position statement.
10/15/14	Review and revision to guideline; consisting of reformatting position statement and updating references.
01/01/15	Revision to guideline; consisting of updating position statement.
10/15/15	Review and revision to guideline; consisting of updating the position statement and references.
11/01/15	Revision: ICD-9 Codes deleted.
01/01/17	Review and revision to guideline; consisting of updating the position statement, administration, precautions and references.
10/15/17	Review and revision to guideline; consisting of updating the position statement and references.
1215/18	Review and revision to guideline; consisting of updating the position statement and references.
11/15/19	Review and revision to guideline; consisting of updating the description, position statement and references.
07/01/20	Revision to guideline; consisting of updating the position statement.
10/01/20	Revision to guideline; consisting of updating the position statement.
04/01/21	Revision to guideline; consisting of updating the position statement.
10/01/22	Review and revision to guideline; consisting of updating the position statement to include Tascenso ODT, and updating description, dosing, and references.
01/01/23	Revision to guideline; consisting of updating the position statement to include generic fingolimod as a preferred generic and removal of Gilenya as a preferred brand.

04/01/23	Review and revision to guideline; consisting of updating the position statement to include a step through generic fingolimod in the continuation criteria for Gilenya.
05/15/23	Revision to guideline; consisting of updating the position statement to include generic teriflunomide as a preferred generic and removal of Aubagio as a preferred brand. Updated list of agents not to be used in combination.
07/15/23	Revision to guideline; consisting of updating the position statement to revise the position statement and dosing for patients weighing 40 kg or less.
11/15/23	Review and revision to guideline; consisting of updating the position statement to include Glatopa and update to warnings.
07/15/24	Update to continuation criteria in the position statement.