Central Nervous System: Multiple Sclerosis Agents, Oral Utilization Management Criteria

Therapeutic Class:	Central Nervous System: Multiple Sclerosis Agents, Oral
Non-Preferred Agents:	Ampyra (dalfampridine), Aubagio (teriflunomide), Bafiertam DR (monomethyl fumarate), Gilenya (fingolimod), Mavenclad (cladribine), Mayzent (siponimod), Ponvory (ponesimod), Tascenso ODT (fingolimod), Tecfidera DR (dimethyl fumarate), Vumerity (diroximel fumarate), Zeposia (ozanimod)
Preferred Agents:	Dalfampridine ER generic, Dimethyl fumarate DR generic, fingolimod 0.5 mg capsule generic, teriflunomide generic
Implementation Date:	12/1/2025
Prepared For:	CT
PDL Status:	Non-preferred
Purpose:	Multiple sclerosis (MS) is an immune-mediated disease of the central nervous system characterized by neurologic damage that can affect any part of the body. Symptoms include, but are not limited to, vision problems, numbness or tingling of the face or body, walking difficulties, spasticity, fatigue, or bladder/bowel problems. The exact cause of MS is unknown; however, genetic, infectious, and environmental factors have been identified as potential contributors to the development of this disease. Clinically isolated syndrome (CIS) refers to the first episode of neurologic symptoms of MS. Relapsing-remitting MS (RRMS) is the most common disease course and is characterized by episodes of new or worsening symptoms (relapses) followed by periods of recovery. RRMS often transitions to secondary progressive MS (SPMS), where disability progression steadily occurs over time, independent of relapses. Primary progressive MS (PPMS) is characterized by worsening neurologic function from the onset of symptoms without early relapses or remissions. Disease-modifying treatments (DMTs) are utilized to reduce the number of relapses, delay the progression of disability, and limit new disease activity. The oral DMTs for MS include sphingosine 1-phosphate receptor modulators (fingolimod, siponimod, ozanimod, and ponesimod), fumaric acid derivatives (dimethyl fumarate, diroximel fumarate, and monomethyl fumarate), as well as cladribine and teriflunomide. All agents are approved for treating relapsing forms of MS, including RRMS, active SPMS, and (except for cladribine) CIS. Ozanimod is also an approved agent for the treatment of ulcerative colitis. Only

	one oral disease-modifying agent, fingolimod, is approved for use in pediatric patients. It should be noted that the sphingosine 1-phosphate receptor modulators have agent-specific monitoring parameters following the first dose. In addition, use of siponimod requires CYP2C9 genotyping. Notably, the approval of monomethyl fumarate, the active metabolite of dimethyl fumarate, was based on bioequivalence to dimethyl fumarate. Dalfampridine is a broad spectrum calcium channel blocker indicated to improve walking in patients with MS. In clinical trials, it demonstrated increase in walking speed. Dalfampridine is contraindicated in moderate or severe renal impairment and patients with a history of seizures.

Table 1. Central Nervous System: Multiple Sclerosis Agents, Oral

Generic Name	Brand Name	Approved Indications	Route of Administration	Generic Availability
Cladribine	Mavenclad®	RRMS, SPMS	PO	N
Dalfampridine	Ampyra®	To improve walking in MS	PO	Y
Dimethyl Fumarate	Tecfidera®	CIS, RRMS, SPMS	PO	Y
Diroximel Fumarate	Vumerity®	CIS, RRMS, SPMS	PO	N
Fingolimod	Gilenya®	CIS, RRMS, SPMS	PO	Y for 0.5 mg strength
	Tascenso ODT™	CIS, RRMS, SPMS	PO	N
Monomethyl Fumarate	Bafiertam®	CIS, RRMS, SPMS	PO	N
Ozanimod	Zeposia®	CIS, RRMS, SPMS, UC	PO	N
Ponesimod	Ponvory™	CIS, RRMS, SPMS	PO	N
Siponimod	Mayzent®	CIS, RRMS, SPMS	PO	N
Teriflunomide	Aubagio®	CIS, RRMS, SPMS	PO	Y

Abbreviations: CIS, clinically isolated syndrome; MS, multiple sclerosis; ODT, orally disintegrating tablet; PO, oral; RRMS, relapsing remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis; UC, ulcerative colitis.

All authorizations must be prescribed in accordance with FDA approved labeling. Use of samples to initiate therapy does not meet step therapy and/or continuation of therapy prior authorization requirements. Prior therapies will be verified through pharmacy claims and/or submitted chart notes.

General Approval Criteria:

- Requested quantity in accordance with FDA approved product labelling
- For specific formulation requests
    - **For brand requests when a therapeutically equivalent generic is preferred:** Provider must provide a documented medical reason the preferred generic formulation cannot be used

- **For generic requests when a therapeutically equivalent brand is preferred:** Provider must provide a documented medical reason the preferred brand formulation cannot be used
- **For non-preferred dosage or formulation requests:** Provider must provide a documented medical reason the preferred dosage or formulation cannot be used

Initial Therapy – All the following must be met for the diagnosis of Multiple sclerosis:

- Prescribed by or in consultation with a neurologist or other specialist familiar with the treated disease state
- Claim is for a preferred agent **OR**
- Patient has a documented diagnosis of CIS (with the exception of Mavenclad) or Multiple Sclerosis **AND** Failure to achieve desired therapeutic outcome with a trial of **ONE** preferred oral (excluding dalfampridine) **OR** injectable MS agent (defined as 30 day trial) **OR** documented adverse drug event/adverse drug reaction or contraindication to preferred products **AND**

Additional Criteria For Mavenclad

- Documentation of all of the following prior to starting each Mavenclad treatment course
  - Standard guideline directed cancer screenings have been completed
  - Pregnancy testing in females of reproductive potential
  - Complete blood count with lymphocytes
  - Tuberculosis screening
  - Hepatitis B and C screening
  - Human immunodeficiency virus (HIV) screening
  - Lack of acute infections
  - Varicella zoster antibody or vaccination status
  - Liver function tests
  - Baseline MRI because of the risk of progressive multifocal leukoencephalopathy (PML)
- Therapy will deny if:
  - Patient has a current malignancy
  - Patient is pregnant
  - Lymphocytes
    - Are not within normal limit prior to first treatment course **OR**
    - Are not at least 800 cells per microliter before initiating the second treatment course
  - Patient has been diagnosed with HIV
  - Patient has active, chronic infections
  - Patient has already received 2 treatment courses and an additional course is requested within 2 years

Additional Criteria for Mayzent, Ponvory, Zeposia

- Documentation of all of the following prior to starting therapy
  - CYP2C9 genotype determination (Mayzent only)
  - Complete blood count with lymphocytes
  - Ophthalmic evaluation
  - Cardiac evaluation (electrocardiogram)
  - Liver function tests
  - Varicella zoster antibody or vaccination status
- Therapy will deny if:
  - Patient has a CYP2C9*3/*3 genotype (Mayzent only)
  - Patient has severe untreated sleep apnea (Zeposia only)

- Is taking a monoamine oxidase inhibitor (Zeposia only)
- Patient has presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker
- Patient has experienced myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or Class III or IV heart failure in the last 6 months

Criteria for Gilenya 0.25 mg

- Patient is 10 years and older and weighs less than or equal to 40 kg. *(Trial and failure of a preferred agent not required)*

Criteria for Tascenso ODT

- For Tascenso ODT 0.25 mg dosing: Patient is 10 years and older and weighs less than or equal to 40 kg. *(Trial and failure of a preferred agent not required)*
- For all other patients, provide documentation of medical reason patient cannot take preferred fingolimod dosage form

For the diagnosis of moderately to severely active ulcerative colitis – all of the following must be met

- Claim is for Zeposia
- Documented diagnosis (listed above)
- Prescribed by or in consultation with a gastroenterologist
- Trial of a preferred tumor necrosis factor inhibitor (TNFi)(30 days) or preferred ustekinumab biosimilar **OR** documented adverse event/adverse reaction or contraindication to TNFi and Ustekinumab biosimilars
- Documentation of all of the following prior to starting therapy
  - Complete blood count with lymphocytes
  - Ophthalmic evaluation
  - Cardiac evaluation (electrocardiogram)
  - Liver function tests
  - Varicella zoster antibody or vaccination status
- Therapy will deny if:
  - Patient has severe untreated sleep apnea
  - Is taking a monoamine oxidase inhibitor
  - Patient has presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker
  - Patient has experienced myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or Class III or IV heart failure in the last 6 months

Non-preferred Age limitations

- Ampyra, Aubagio, Bafiertam, Mavenclad, Mayzent, Ponvory, Tecfidera, Vumerity, Zeposia: 18 years and older
- Gilenya, Tascenso ODT: 10 years and older

Claim Exceeds Maximum Dosing Limitations for Non-preferred Agents

Drug	Daily Dosing Limitation
AMPYRA ER 10 MG TABLET	2 tablets per day
AUBAGIO 7 MG TABLET	1 tablet per day
AUBAGIO 14 MG TABLET	1 tablet per day
BAFIERTAM DR 95 MG CAPSULE	4 capsules per day
GILENYA 0.5 MG CAPSULE	1 capsule per day
GILENYA 0.25 MG CAPSULE	1 capsule per day
MAYZENT 0.25 MG TABLET	5 tablets per day
MAYZENT 1 MG TABLET	1 tablet per day
MAYZENT 2 MG TABLET	1 tablet per day
PONVORY 20 MG TABLET	1 tablet per day
TASCENSO ODT 0.25 MG TABLET	1 tablet per day
TASCENSO ODT 0.5 MG TABLET	1 tablet per day
TECFIDERA DR 120 MG CAPSULE	2 capsules per day
TECFIDERA DR 240 MG CAPSULE	2 capsules per day
VUMERITY DR 231 MG CAPSULE	4 capsules per day
ZEPOSIA 0.92 MG CAPSULE	1 capsule per day

Initial PA length: 4 months for Mavenclad, 1 year for other agents

Exclusion Criteria: Approval criteria not met

Continuation Therapy: Documented compliance on current therapy regimen **AND**
Documented continued clinical benefit **AND**

- For specific formulation requests
    - **For brand requests when a therapeutically equivalent generic is preferred:** Provider must provide a documented medical reason the preferred generic formulation cannot be used
    - **For generic requests when a therapeutically equivalent brand is preferred:** Provider must provide a documented medical reason the preferred brand formulation cannot be used

- **For non-preferred dosage or formulation requests:** Provider must provide a documented medical reason the preferred dosage or formulation cannot be used

Continuation Length: 4 months for Mavenclad, 1 year for other agents

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Revision History

Date	Version	Revisions
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