MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY:	Multiple Sclerosis	**P&T DATE:**	03/11/2025
CLASS:	Neurologic Disorders	**REVIEW HISTORY:** (*month/year*)	6/24, 1/24, 12/22, 9/21, 5/20, 2/19, 12/17, 12/16,9/15, 5/13
LOB:	MCL		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the Health Plan of San Joaquin/Mountain Valley Health Plan (Health Plan) Pharmacy and Therapeutic Advisory Committee.

Effective 1/1/2022, the Pharmacy Benefit is regulated by Medi-Cal Rx. Please visit https://medi-calrx.dhcs.ca.gov/home/ for portal access, formulary details, pharmacy network information, and updates to the pharmacy benefit. All medical claims require that an NDC is also submitted with the claim. If a physician administered medication has a specific assigned CPT code, that code must be billed with the correlating NDC. If there is not a specific CPT code available for a physician administered medication, the use of unclassified CPT codes is appropriate when billed with the correlating NDC.

OVERVIEW

The purpose of this coverage policy is to review the available agents (Table 1) and distinguish where the medications may be billed to. For agents listed for coverage under the medical benefit, this coverage is specific to outpatient coverage only (excludes emergency room and inpatient coverage).

Table 1: Available Multiple Sclerosis Agents:

CPT Code	Generic Name (Brand Name)	Available Strengths	Pharmacy Benefit	Outpatient Medical Benefit (Restrictions)
J1830	Interferon β -1b (Betaseron)	0.3 Mg Subcutaneous Kit	Yes	Yes (PA)
J1826	Interferon β -1a (Avonex)	30 Mcg Intramuscular Kit	Yes	Yes (PA)
Q3028	Interferon β -1a (Rebif)	22 Mcg/0.5 mL SQ Syringe, 44 Mcg/0.5 mL SQ Syringe	Yes	Yes (PA)
J1595	Glatiramer acetate (Copaxone, Glatopa)	20mg/mL Syringe/Kit 40 mg/mL Syringe/Kit	Yes	Yes (PA)
--	Fingolimod (Gilenya)	0.5 mg Capsule	Yes	No
--	Teriflunomide (Aubagio)	7 mg, 14mg Tablet	Yes	No
--	Dimethyl Fumarate (Tecfidera)	120mg, 240mg DR Capsule	Yes	No
--	Diroximel Fumarate (Vumerity)	231 mg Capsule	Yes	No
J9293	Mitoxantrone (Novantrone)	2mg/mL IV Soln	Yes	Yes (PA)
J2323	Natalizumab (Tysabri)	300mg/15mL IV Soln	Yes	Yes (PA)
Q5134	Natalizumab-sztn (Tyruko)	300mg/15mL IV Soln	Yes	Yes (PA)
J0202	Alemtuzumab (Lemtrada)	12mg/1.2mL Vial	Yes	Yes (PA)
J9302	Ofatumumab (Kesimpta)	20mg/0.4mL Auto-injector	Yes	No
J2350	Ocrelizumab (Ocrevus)	300 mg/10 ml IV Soln	Yes	Yes (PA)
--	Ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo)	920 mg/23,000 units per 23 mL SQ Soln	Yes	Yes (PA)
J2329	Ublituximab-xiiy (Briumvi)	150mg/6mL IV Soln	Yes	Yes (PA)
--	Dalfampridine (Ampyra)	10mg ER Tablet	Yes	No
--	Peginterferon β -1a (Plegridy)	63mcg/0.5 ml Starter Pack 125 mcg/0.5ml syringe	Yes	No

PA = Prior Authorization

Clinical Justification:

Interferon and glatiramer have a long history of use, and proven safety and tolerability profile, which is why they are listed as a first line option for Health Plan members. Newer agents, such as Tecfidera, Aubagio, and Gilenya have more risk of potentially serious adverse effects. Though they are more convenient to administer (oral), they have had less time on the market, and will require robust post-marketing data to ensure patient safety. These oral agents for multiple sclerosis are covered through the pharmacy benefit. Both Novantrone and Tysabri/Tyruko are restricted as last line disease modifying therapy, due to the risks involved with these drugs. They both have black box warnings. Novantrone for myocardial toxicity, and Tysabri for Progressive Multifocal Leukoencephalopathy. Both are potentially fatal conditions. Lemtrada and Ocrevus/Ocrevus Zunovo are both reserved as third line options as well due to their mixed efficacy results and potential safety concerns. However, as Ocrevus/Ocrevus Zunovo are high-efficacy therapies there is criteria to bypass the use of other agents as certain patient populations may benefit from starting with this therapy to achieve optimal control of disease activity. Ocrevus/Ocrevus Zunovo and Briumvi are both anti-CD20 monoclonal antibodies so the criteria for Briumvi is consistent with the FDA labeling and similar to Ocrevus for the treatment of RMS.

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for agents with medical benefit restrictions. This coverage criteria has been reviewed and approved by the Health Plan Pharmacy & Therapeutics (P&T) Advisory Committee. For agents that do not have established prior authorization criteria, Health Plan will make the determination based on Medical Necessity criteria as described in Health Plan Medical Review Guidelines (UM06).

Interferons

Interferon β -1b (Betaseron), Interferon β -1a (Avonex), Interferon β -1a (Rebif)

- ❒ **Coverage Criteria:** Prior Authorization required unless used for Multiple Sclerosis and the provider is in network.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** None

Biologic

Glatiramer (Glatopa)

- ❒ **Coverage Criteria:** Prior Authorization required unless used for Multiple Sclerosis and the provider is in network.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** None

Antineoplastic Agents

Mitoxantrone (Novantrone)

- ❒ **Coverage Criteria:** Reserved as third line therapy for multiple sclerosis (MS) behind [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya, Aubagio, Tecfidera, or Vumerity due to increased risk of developing progressive multifocal leukoencephalopathy (PML). Documentation of a negative anti-JCV antibody test is required at initiation and annually for continuation.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis. Additionally, patient must have documented treatment failure of the above two categories (1st line and 2nd line MS drugs).

Alemtuzumab (Lemtrada)

- ❒ **Coverage Criteria:** Reserved for patients with relapsing remitting multiple sclerosis (RRMS) with inadequate treatment response to one drug from the following two categories: [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya, Aubagio, Tecfidera, or Vumerity. Members must have no previous history of malignancy, and documentation of negative HIV, HBV, HCV, and TB tests.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis. Additionally, patient must have documented treatment failure of the above two categories (1st line and 2nd line MS drugs). Documentation that the member is negative for latent or active infections.
- ❒ **Other Notes:** Daclizumab (Zinbryta) was discontinued by the manufacturer in March 2018 due to the drug's concerning benefit/risk profile.

Anti-CD20 Monoclonal Antibodies

Ocrelizumab (Ocrevus), Ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo)

- ❒ **Coverage Criteria:**
  - **For patients with Relapsing MS (RMS), Ocrevus and Ocrevus Zunovo are reserved for patients who meet all of the following criteria:**
    - [A] Patient must either:
      - [1] Have had an inadequate treatment response to one drug from each of the following two categories: [i] Betaseron / Avonex / Rebif / Glatopa, AND [ii] Gilenya, Aubagio, Tecfidera, or Vumerity; OR
      - [2] Require high efficacy therapy due to meeting one of the following criteria:
        - EDSS score of ≥ 4 at 5 years of onset of the disease
        - EDSS score ≥ 6 by 40 years of age
        - Multiple relapses (two or more) in the previous year
        - One relapse in the previous year with poor prognosis due to incomplete remission and/or followed by disability
        - A minimum of 2 brain magnetic resonance imaging (MRI) studies with new lesions or increase in the size of the lesions in T2, or lesions that enhance with gadolinium despite adherence to MS treatment for at least 6 months
        - ≥ 2 gadolinium-enhancing lesions on T1-weighted sequences or ≥ 9 lesions on T2-weighted sequences
        - MRI lesions in the infratentorial region or spinal cord
        - Multiple factors indicating poor prognosis (such as biomarkers, demographic factors, clinical factors, and/or radiological factors)
    - [B] Prescribed by a neurologist
    - [C] Lab documentation of a quantitative serum immunoglobulin test and a negative Hepatitis B Virus (HBV), at initiation
  - For patients with **Primary Progressive Multiple Sclerosis (PPMS)**, members must documentation of a quantitative serum immunoglobulin test and negative HBV test at initiation. Prescription must be written by a neurologist and patient must have chart notes showing a diagnosis of PPMS.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis members and must have a quantitative serum immunoglobulin test and negative HBV test at initiation. Additionally, patient must have documented treatment failure of the above two categories (1st line and 2nd line MS drugs) OR meet criteria for high efficacy therapy.

Ublituximab-xiiy (Briumvi)

- ❒ **Coverage Criteria:**
  - **For patients with Relapsing MS (RMS), Briumvi is reserved for patients who meet all of the following criteria:**
    - [A] Patient must either:
      - [1] Have had an inadequate treatment response to one drug from each of the following two categories: [i] Betaseron / Avonex / Rebif / Glatopa, AND [ii] Gilenya, Aubagio, Tecfidera, or Vumerity; OR
      - [2] Require high efficacy therapy due to meeting one of the following criteria:
        - EDSS score of ≥ 4 at 5 years of onset of the disease
        - EDSS score ≥ 6 by 40 years of age
        - Multiple relapses (two or more) in the previous year
        - One relapse in the previous year with poor prognosis due to incomplete remission and/or followed by disability
        - A minimum of 2 brain magnetic resonance imaging (MRI) studies with new lesions or increase in the size of the lesions in T2, or lesions that enhance with gadolinium despite adherence to MS treatment for at least 6 months
        - ≥ 2 gadolinium-enhancing lesions on T1-weighted sequences or ≥ 9 lesions on T2-weighted sequences
        - MRI lesions in the infratentorial region or spinal cord
        - Multiple factors indicating poor prognosis (such as biomarkers, demographic factors, clinical factors, and/or radiological factors)
    - [B] Prescribed by a neurologist
    - [C] Lab documentation of a quantitative serum immunoglobulin test and a negative Hepatitis B Virus (HBV), at initiation
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis members and must have a quantitative serum immunoglobulin test and a negative HBV test at initiation. Additionally, patient must have documented treatment failure of the above two categories (1st line and 2nd line MS drugs) OR meet criteria for high efficacy therapy.

Selective Adhesion-Molecule Inhibitor

Natalizumab (Tysabri), Natalizumab-sztn (Tyruko)

- ❒ **Coverage Criteria:** Reserved as third line therapy for MS behind [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya, Aubagio, Tecfidera, or Vumerity due to increased risk of developing progressive multifocal leukoencephalopathy (PML). Documentation of a negative anti-JCV antibody test is required at initiation and annually for continuation.
- ❒ **Limits:** None

  Required Information for Approval: Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis. Additionally, patient must have documented treatment failure of the above two categories (1st line and 2nd line MS drugs).

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REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	MS Drug Class Review 5-21-2013.docx	5/2013	Jonathan Szkotak, PharmD BCACP
Updated Policy	Tecfidera Monograph 2014-09-16.docx	9/2014	Jonathan Szkotak, PharmD BCACP
Updated Policy	HPSJ Coverage Policy - Neurologic Disorders - Multiple Sclerosis 2015-09.docx	9/2015	Jonathan Szkotak, PharmD BCACP
Updated Policy	HPSJ Coverage Policy - Neurologic Disorders - Multiple Sclerosis 2016-12.docx	12/2016	Johnathan Yeh, PharmD
Updated Policy	HPSJ Coverage Policy - Neurologic Disorders - Multiple Sclerosis 2017-12.docx	12/2017	Johnathan Yeh, PharmD
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Review of Policy	Multiple Sclerosis	12/2022	Matthew Garrett, PharmD
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Note: All changes are approved by the Health Plan P&T Committee before incorporation into the utilization policy