MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

Health Plan of San Joaquin

POLICY:	Multiple Sclerosis	**P&T DATE:**	9/14/21
CLASS:	Neurologic Disorders	**REVIEW HISTORY:** (*month/year*)	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 HPSJ Pharmacy and Therapeutic Advisory Committee.

OVERVIEW

Table 1: Available Multiple Sclerosis Agents:

Generic	Brand	Available Strengths	Dosing	Avg Cost/Mth	Form Status	HPSJ Formulary Position
Interferon β - 1b (SC)	Betaseron	0.3 Mg Subcutaneous Kit	0.25 mg SQ QOD	$6,816.01		1st line
Interferon β - 1a (IM)	Avonex	30 Mcg Intramuscular Kit	30 mcg IM q week	$7,126.88		1st line
Interferon β - 1a (SC)	Rebif	22 Mcg/0.5 mL SQ Syringe, 44 Mcg/0.5 mL SQ Syringe	22-44 mcg SQ 3xweekly	$8,520.50		1st line
Glatiramer acetate	Generic Copaxone	20mg/mL Syringe 40 mg/mL Syringe	20 mg SQ daily 40 mg SQ TIW	$1,562.09 $1,519.25		1st line
	Brand Copaxone	20mg/mL Syringe 40 mg/mL Syringe		$830.41		NF
	Glatopa	20mg/mL Syringe Kit 40 mg/mL Syringe Kit		$1,562.09		1st line
Fingolimod	Gilenya	0.5 mg Capsule	0.5 mg po daily	$8,872.03		2nd line
Teriflunomide	Aubagio	7 mg, 14mg Tablet	7-14 mg po daily	$7,927.10		2nd line
Dimethyl Fumarate	Tecfidera	120mg, 240mg DR Capsule	240mg BID	$3,000.30		2nd line
Diroximel Fumarate	Vumerity	231 mg Capsule	462mg BID	$9,026.40	PA	3rd line
Mitoxantrone	Novantrone	2mg/mL IV Soln	12 mg/m^2 IV q3 months	$408.00*		3rd line
Natalizumab	Tysabri	300mg/15mL IV Soln	300 mg IV over hour q4 weeks	$7,675.50‡		3rd line
Alemtuzumab	Lemtrada	12mg/1.2mL Vial	12mg IV daily for 5 days repeated in 1 year for 3 days	$27,484.80‡		3rd line
Ofatumumab	Kesimpta	20mg/0.4mL Auto-injector	20mg once weekly for 3 doses; then 20mg once monthly starting at week 4	$8,549.00		1st or 3rd line
Ocrelizumab	Ocrevus	300 mg/10 ml IV Soln	300 mg on day 1, followed by 300 mg 2 weeks later; then 600 mg q6 months	$39,000.00‡		3rd line
Dalfampridine	Dalfampridine	10mg ER Tablet	10mg BID	$57.45		N/A
	Ampyra	10mg ER Tablet		--		
Peginterferon β -1a (SC)	Plegridy	63mcg/0.5 ml Starter Pack 125 mcg/0.5ml syringe	125mcg q 2 weeks	--	NF	NF

*Medication is administered every 3 months. AWP pricing is based on BSA of 1.9m^2. Total cumulative dose is 140mg/m^2 per lifetime. Currently there are no patients at HPSJ utilizing this drug. .

RRMS = Relapsing Remitting Multiple Sclerosis, SPMS = Secondary Progressive Multiple Sclerosis, PRMS = Primary Relapsing Multiple Sclerosis, BBW = Black Box Warning, AML = Acute Myelogenous Leukemia, LVEF = Left ventricular ejection fraction, CHF = Congestive Heart Failure, PML = Progressive Multifocal leukoencephalopathy SJS = Stevens Johnson's Syndrome F = Formulary. PA = PA Required.

Clinical Justification:

All multiple sclerosis drugs are restricted to use by neurologists. This is to ensure that patients are being monitored for disease progression and side effects by a specialist. Interferon and glatiramer have a long history of use, and proven safety and tolerability profile, which is why they are first line therapy for HPSJ 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. Both Novantrone and Tysabri 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 is reserved for last line due to the same reason, mixed efficacy results and potential safety concerns.

Triage:

1. Appropriate diagnosis
2. Prescribed by a neurologist
3. List of previous MS drugs tried, reaction, type/severity, or documentation of disease progression in chart notes.

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

Interferons

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

- ❒ **Coverage Criteria:** Restricted to patients with a verified diagnosis of MS with therapy initiated by a neurologist.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis.

Biologic

Glatiramer (Glatopa)

- ❒ **Coverage Criteria:** Restricted to patients with a verified diagnosis of MS with therapy initiated by a neurologist.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis.
- ❒ **Notes:** Copaxone 20mg and 40mg are non-formulary.

Sphingosine 1-Phosphate (S1P) Receptor Modulator

Fingolimod (Gilenya)

- ❒ **Coverage Criteria:** Reserved for second line therapy after treatment failure of Avonex, Glatopa, Rebif, or Betaseron. Restricted to patients with a verified diagnosis of MS with therapy initiated by a neurologist.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis, and must have pharmacy fill history, and chart note documentation of treatment failure of one First-Line Disease Modifying Treatment.

Pyrimidine Synthesis Inhibitor

Teriflunomide (Aubagio)

- ❒ **Coverage Criteria:** Reserved for second line therapy after treatment failure of Avonex, Glatopa, Rebif, or Betaseron. Restricted to patients with a verified diagnosis of MS with therapy initiated by a neurologist.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis, and must have pharmacy fill history, and chart note documentation of treatment failure of one First-Line Disease Modifying Treatment.

Fumaric Acid Derivative

Dimethyl Fumarate (Tecfidera)

- ❒ **Coverage Criteria:** Reserved for second line therapy after treatment failure of Avonex, Glatopa, Rebif, or Betaseron. Restricted to patients with a verified diagnosis of MS with therapy initiated by a neurologist.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis, and must have pharmacy fill history, and chart note documentation of treatment failure of one First-Line Disease Modifying Treatment.

Diroximel Fumarate (Vumerity)

- ❒ **Coverage Criteria:** Reserved for patients with relapsing-remitting multiple sclerosis who have tried and failed or are intolerant to three months of compliant use of Tecfidera (dimethyl fumarate).
- ❒ **Limits:** Limited to 120 tablets per 30 days.
- ❒ **Required Information for Approval:** Fill history of Tecfidera for three consecutive months and chart notes documenting either progression of multiple sclerosis or intolerance.

Antineoplastic Agents

Mitoxantrone (Novantrone)

- ❒ **Coverage Criteria:** Reserved as third line therapy for MS behind [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya or Aubagio or Tecfidera 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 MS with inadequate treatment response to one drug from the following two categories: [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya, Aubagio, or Tecfidera. 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.

Ofatumumab (Kesimpta)

- ❒ **Coverage Criteria:** Reserved for adult patients with relapsing remitting multiple sclerosis, clinically isolated syndrome, or active secondary progressive disease who meet one of the following:
  - Inadequate treatment response to one drug from the following two categories: [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya or Tecfidera. Must NOT have an active Hepatitis B infection and must have serum immunoglobulins screening prior to starting the first dose. Must be seen by a neurologist. Restricted to specialty pharmacy.
  - Adult patient who is 40 years of age or younger, has had at least 1 relapse in the past 24 months, has an EDSS score of 3 or more, and diagnosed with multiple sclerosis for at least 5 years. Must NOT have an active Hepatitis B infection and must have serum immunoglobulins screening prior to starting the first dose. Must be seen by a neurologist. Must have a baseline gadolinium-enhanced MRI result. Restricted to specialty pharmacy.
- ❒ **Limits:**
  - Loading Dose: Limited to 3 syringes for the first 28 days.
  - Maintenance Dose**:** Limited to 1 syringe per 28 days following the loading dose.
- ❒ **Required Information for Approval:** Chart notes documenting treatment history, relapse history, disease history, patient's EDSS score, Hepatitis B screening, serum immunoglobulins screening, and gadolinium-enhanced MRI scan.

Ocrelizumab (Ocrevus)

- ❒ **Coverage Criteria:**
  - **For patients with Relapsing MS (RMS), Ocrevus is reserved for patients with inadequate treatment response to one drug from the following two categories:** [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya, Aubagio, or Tecfidera. Prescription must be written by a neurologist and members must have no previous history of malignancy, and documentation of negative HIV, HBV, HCV, and TB tests. It must also be documented that the member is negative for latent or active infections and a negative anti-JCV antibody test is required at initiation and annually for continuation.
  - For patients with **Primary Progressive Multiple Sclerosis (PPMS)**, members must have no previous history of malignancy, and documentation of negative HIV, HBV, HCV, and TB tests. Prescription must be written by a neurologist and patient must have chart notes showing a diagnosis of PPMS.

Additionally, there must have documentation that the member is negative for latent or active infections, and 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). Documentation that the member is negative for latent or active infections and a negative anti-JCV antibody test is required at initiation and annually for continuation.

Selective Adhesion-Molecule Inhibitor

Natalizumab (Tysabri)

- ❒ **Coverage Criteria:** Reserved as third line therapy for MS behind [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya or Aubagio or Tecfidera 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).

Potassium Channel Blockers

Dalfampridine (Ampyra)

- ❒ **Coverage Criteria:** It is reserved for patients who meet ALL of the following: [1] Diagnosis of MS, [2] Receiving concurrent disease modifying therapy, [3] Prescribed by a neurologist, [4] The patient is ambulatory with a 25 foot timed-walk test between 8-45 seconds, [5] No history of seizures, [6] Creatinine clearance >=50 ml/min. Initial approval is for 60 days only. For continuation beyond 60 days, documentation of at least 20% improvement of the 25-foot timed-walk test from baseline is required.
- ❒ **Limits: None**
- ❒ **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis. Chart notes must also document the patient's 25-foot walk test, and creatinine clearance of greater than 50 mL/min.

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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
Updated Policy	HPSJ Coverage Policy - Neurologic Disorders - Multiple Sclerosis 2019-02.docx	2/2019	Matthew Garrett, PharmD
Updated Policy	Multiple Sclerosis.docx	5/2020	Matthew Garrett, PharmD
Updated Policy	Multiple Sclerosis.docx	9/2021	Matthew Garrett, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy