MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

Health Plan of San Joaquin

POLICY:	Multiple Sclerosis	**P&T DATE:**	12/14/2017
CLASS:	Neurologic Disorders	**REVIEW HISTORY:** (*month/year*)	12/16, 9/15, 9/14, 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	$7,462.56	PA	1st line
Interferon β -1a (IM)	Avonex	30 Mcg Intramuscular Kit	30 mcg IM q week	$7,544.40		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	$8248.80		1st line
Glatiramer acetate	Glatopa	20mg/mL Syringe Kit	20 mg SQ daily	$6232.50ǂ		1st line
Glatiramer acetate	Copaxone	20mg/mL Syringe Kit 40mg/mL Syringe Kit	20 mg SQ daily 40mg TIW	$6232.50		1st line
Fingolimod	Gilenya	0.5 mg,	0.5 mg po daily	$6,894.70		2nd line
Teriflunomide	Aubagio	7 mg, 14mg,	7-14 mg po daily	$7,933.80		2nd line
Dimethyl Fumarate	Tecfidera	120mg, 240mg	240mg BID	$8,183.40		2nd line
Mitoxantrone	Novantrone	2mg/mL	12 mg/m^2 IV q3 months	$325.70*		3rd line
Natalizumab	Tysabri	300mg/15mL IV Soln	300 mg IV over 1 hour q4 weeks	$7,200.00ǂ		3rd line
Daclizumab	Zinbryta	150mg/mL Syringe	150mg SQ once monthly	$8,683.80ǂ		3rd line
Alemtuzumab	Lemtrada	12mg/1.2mL Vial	12mg IV daily for 5 days repeated in 1 year for 3 days	$25,522.32		3rd line
Ocrelizumab	Ocrevus	300mg/10ml Vial	600mg IV q 6 months	$6500.00		1st/3rd line
Dalfampridine	Ampyra	10mg Tablet	10mg BID	$2,694.06		N/A
Peginterferon β -1a (SC)	Plegridy	63mcg/0.5 ml Starter Pack 125 mcg/0.5ml syringe	125mcg q 2 weeks	$7,544.40	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. ǂAWP data.

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 and Zinbryta are 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 HSPJ Medical Review Guidelines (UM06).

1st Line Disease Modifying Therapy

Interferon β -1b (Betaseron), Interferon β -1a (Avonex), Interferon β -1a (Rebif), Glatiramer (Glatopa), Ocrelizumab (Ocrevus)

- ❒ **Coverage Criteria:** Restricted to patients with a verified diagnosis of MS with therapy initiated by a neurologist. Avonex, Copaxone, Rebif, and Betaseron are first line therapy for multiple sclerosis. Ocrevus 1st line is reserved for patients with Primary Progressive Multiple Sclerosis.
- ❒ **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.

2nd Line Disease Modifying Therapy

Fingolimod (Gilenya), Teriflunomide (Aubagio), 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.

3rd Line Disease Modifying Therapy

Mitoxantrone (Novantrone), Natalizumab (Tysabri),

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

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

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.

REFERENCES

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3. Montalban, X, Hauser, SL, Kappos, L; ORATORIO Clinical Investigators. Ocrelizumab versus placebo in primary progressive multiple sclerosis. N Engl J Med. 2017;376(3):209-220.
4. National Institute for Health and Care Excellence. Multiple sclerosis in adults: management. http://nice.org.uk/guidance/cg186. Published October 8, 2014
5. Goodin DS, Cohen BA, O'Connor P, Kappos L, Stevens JC, Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: the use of natalizumab (Tysabri) for the treatment of multiple sclerosis (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology [Internet]. 2008 Sep 2;71(10):766-73
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7. Cortese, I. et al. "Evidence-Based Guideline Update: Plasmapheresis in Neurologic Disorders: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology." Neurology 76.3 (2011): 294–300. PMC. Web. 21 Nov. 2017.
8. Selmaj K, Barkhof F, Belova AN et al (2017) Switching from branded to generic glatiramer acetate: 15-month GATE trial extension results. Mult Scler. doi:10.1177/1352458516688956

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

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