DRUG DETERMINATION POLICY

Title: DDP-35 Multiple Sclerosis (MS) Agents

Effective Date: 10/26/22

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Multiple Sclerosis agents are specialty drugs indicated for several specific subtypes and are associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. Dalfampridine oral [must meet all listed below]:

   A. Age: at least 18 years.

   B. Prescriber: neurologist.

   C. Diagnosis and severity [must meet all listed below]:

      1. Multiple sclerosis with documented difficulty walking, resulting in significant limitations of activities of daily living.

      2. Walk-speed [must meet both listed below]:

         a. Clinical notes documenting three measurements and average score.

         b. Timed 25-foot walk speed (T25FW): baseline 25 feet in 8 to 45 seconds.

D. Other therapies: no prior treatment and failure with dalfampridine (non-responder).

E. Dosage regimen: 10 mg oral twice daily.

F. Approval.

1. Initial approval: four months.

2. Re-approval: six months [must meet all listed below]:

a. Responder: shows benefit after the initial four-month trial period while on medication.

b. Timed 25-foot walk speed (T25FW): improved or maintained over 20 percent above baseline.

c. Significant limitations in activities of daily living: improved or resolved because of increased speed of ambulation as documented in clinical notes.

G. Exclusions:

1. History of seizures.

2. Moderate to severe renal impairment (creatinine clearance below 50ml/minute).

II. Mavenclad oral (cladribine) [must meet all below]:

A. Age: at least 18 years.

B. Prescriber: neurologist.

C. Disease and severity [must meet both listed below]:

1. Relapsing form of multiple sclerosis: relapsing remitting disease or active secondary progressive disease.

2. Relapses: at least one relapse in the past year.

D. Other therapies: contraindication, inadequate response indicated by significant disease flare(s) or significant adverse effect to two other medications indicated for the treatment of multiple sclerosis.

E. Dosage regimen:

1. Total dose: 3.5mg per Kg oral over two years.

2. Courses:

a. Course one: 1.75mg per Kg over two cycles; each cycle lasting 4-5 days (maximum dose 20mg per day); second cycle 23 to 27 days after last day of first cycle.

b. Course two: 1.75mg per Kg over two cycle starting cycle one at least 43 weeks after the last day of course one; second cycle 23-27 days after last day of first cycle.

F. Approval:

1. Initial: course one for three months.

2. Re-approval: course two for three months at least 43 weeks after the end of course one.

G. Exclusions:

1. Diagnosis of clinically isolated syndrome.

2. Presence of current malignancy.

3. Pregnant women, and women and men of reproductive potential who do not plan to use effective contraception during Mavenclad treatment and for six months after the last dose of treatment.

4. Human Immunodeficiency Virus infection.

5. Active chronic infections (e.g., hepatitis or tuberculosis).

6. Women breastfeeding during Mavenclad treatment and ten days after last dose.

III. Ocrevus IV (ocrelizumab) [must meet all listed below]:

A. Age: at least 18 years.

B. Prescriber: neurologist.

C. Disease and severity:

1. Multiple sclerosis, relapsing or primary progressive.

D. Other therapies: contraindication, inadequate response indicated by significant disease flare(s) or significant adverse effect to one of each listed below:

1. Kesimpta SQ (Ofatumumab).

2. One other preferred formulary agent.

E. Dosage regimen:

1. 300 mg on day 1, followed by 300 mg 2 weeks later; subsequent doses of 600 mg are administered once every 6 months (beginning 6 months after the first 300 mg dose).

F. Approval:

1. Initial: 6 months (3 doses).

2. Re-approval: 1 year (2 doses).

G. Exclusions:

1. Concomitant therapy. Must be used as single agent therapy.

2. Active infection.

IV. Tysabri IV (natalizumab) [must meet all listed below]:

A. Age: at least 18 years.

B. Prescriber: neurologist.

C. Disease and severity:

1. Patient has been diagnosed with a relapsing form of multiple sclerosis [i.e. relapsing remitting disease (RRMS), active secondary progressive disease (SPMS), or clinically isolated syndrome (CIS).

D. Other therapies: contraindication, inadequate response indicated by significant disease flare(s) or significant adverse effect to one of each listed below:

1. Kesimpta SQ (Ofatumumab).

2. One other preferred formulary agent.

E. Dosage regimen:

1. 300 mg infused over 1 hour every 4 weeks.

F. Approval:

1. Initial: 6 months.

2. Re-approval: 1 year.

G. Exclusions:

1. Concomitant therapy. Must be used as single agent therapy.

2. Active infection.

V. Appropriate medication use [must meet one listed below]:

A. FDA approval status [must meet one listed below]:

1. FDA approved: product, indication, and/or dosage regimen.

2. Non-FDA approved: compendium support (Lexicomp™) for use of a drug for a non-FDA approved indication or dosage regimen.

B. Place in therapy: sequence of therapy supported by national or international accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

4.0 Coding:

COVERED CODES				
Code	**Brand Name**	**Generic Name**	**Billing Units (1 unit)**	**Prior Approval**
J2350	Ocrevus	ocrelizumab	1 mg	Y
J2323	Tysabri	natalizumab	1 mg	Y

5.0 References, Citations & Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Ampyra, Mavenclad, Ocrevus, Tysabri accessed October 2022.
2. Disease modifying treatment of relapsing-remitting multiple sclerosis in adults. UpToDate **[**internet] Accessed May 2021.
3. Effects of dalfampridine Extended-release Tablets on 6-minute walk distance in patients with MS: A post hoc analysis of a double-blind, placebo-controlled trial. Clinical Therapeutics 2015:37(12);2780-87.
4. Assessing dalfampridine efficacy in the physician's office. Multiple Sclerosis Journal 2014:20(1);24-26.
5. Timed 25-foot walk. American Academy of Neurology 2013:80;1509-17.
6. Challenge of progressive multiple sclerosis therapy. www.co-neurology.com 2017; 30(3):237-240.

6.0 Appendices:

See page 6.

7.0 Revision History:

Original Effective Date: 08/26/2010

Next Review Date: 05/26/2023

Revision Date	Reason for Revision
8/19	Moved to new form; replaced abbreviations
4/20	Annual review; modified instruction and other therapies language; replaced abbreviations; approved at June P&T Committee meeting.
5/21	Annual review: clarified criteria instructions, removed abbreviations, clarified duration of other therapies, clarified purpose, added appropriate therapy
04/22	Annual Review; added compendium to Appropriate use section
11/22	Added Ocrevus and Tysabri with Kesimpta step after rebates review.

Appendix I: Patient Safety and Monitoring

Drug	Adverse Reactions	Monitoring & Contraindications	Requirements
Ampyra dalfampridine	• Central Nervous System : asthenia (7%), balance disorder (5%), dizziness (7%), headache (7%), insomnia (9%) • Gastrointestinal: nausea (7%) • Miscellaneous: urinary tract infection (12%) • Pregnancy: adverse events seen in animal repro. studies (reduced growth and death)	• Lab: creatinine clearance pre and annually	• Medication guide
Mavenclad cladribine	• Central Nervous System: headache (25%) • Gastrointestinal: nausea (10%) • Hematology/Oncology: lymphocytopenia (24-87%), bone marrow depression (34%), reduced Hgb, reduced platelets. • Hypersensitivity: reaction (11%) • Infection: infection (49%) • Respiratory: upper respiratory infection (38%)	• Labs: lymphocyte count (prior, 2 and 6 months. post), liver function tests (prior and as needed) • Infections: signs and symptoms; HIV, Hepatitis B, Hepatitis C, Varicellazoster virus status (prior to treatment) • Pregnancy test • Progressive multifocal leukoencephalopathy: magnetic resonance imaging • Cancer: screening	• Medication guide must be dispensed
Ocrevus Ocrelizumab	• Dermatologic: Skin infection (14%) • Hematologic & oncologic: Decreased neutrophils (13%), decreased serum immunoglobulins (≤17%) • Hypersensitivity: Infusion-related reaction (34% to 40%) • Infection: Infection (58% to 70%) • Respiratory: Upper respiratory tract infection (40% to 49%)	• Hepatitis B virus screening	
Tysabri natalizumab	• Dermatologic: Skin rash (6% to 12%) • Gastrointestinal: Abdominal distress (11%), gastroenteritis (11%) • Genitourinary: Urinary tract infection (3% to 21%) • Infection: Influenza (12%) • Nervous system: Depression (19%), fatigue (10% to 27%), headache (32% to 38%) • Neuromuscular & skeletal: Arthralgia (8% to 19%), back pain (12%), limb pain (16%)	• Symptoms of hepatotoxicity • Radiographic signs of PML periodically	• Baseline brain MRI scan