BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 5/16/19**
SECTION: DRUGS	**LAST REVIEW DATE: 5/16/19**
	LAST CRITERIA REVISION DATE:
	ARCHIVE DATE:

MAVENCLAD® (cladrabine) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Mavenclad (cladrabine) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in Neurology or is in consultation with a Neurologist

2. Individual is 18 years of age or older

3. A confirmed diagnosis of **ONE** of the following:
   - Relapsing forms of multiple sclerosis (MS), including relapsing-remitting disease and active secondary progressive disease such as:
     - Relapsing-remitting MS (RRMS)
     - Secondary-progressive MS (SPMS)
     - Progressive-relapsing MS (PRMS)

4. Individual does not have clinically isolated syndrome (CIS)

5. Individual has failure, contraindication or intolerance to at least 2 alternate drug indicated for the treatment of MS

6. **ALL** of the following tests have been completed before initiation of **EACH** Treatment Course with continued monitoring as clinically appropriate:
   - Cancer screening that follows standard screening guidelines for breast, cervical, colorectal, endometrial, lung , prostate, or other type
   - Negative pregnancy test in a woman of child bearing age
   - Complete blood count with differential
   - Lymphocytes must be within normal limits before 1st treatment course and must be at least 800 cells per microliter before 2nd treatment course
   - A baseline (within 3 months) magnetic resonance imaging prior to the first treatment
   - Serum aminotransferase, alkaline phosphatase, and total bilirubin
   - Individual does not have HIV infection
   - TB screening, if positive, delay Mavenclad (cladrabine) until infection has been treated
   - Hepatitis B & C screening, if positive, delay Mavenclad (cladrabine) until infection has been treated
   - Evaluate for acute infection, delay treatment until any active infection is fully controlled
   - Varicella zoster virus antibody negative individuals must be vaccinated
   - Any needed immunizations that are recommended by immunization guidelines must be given prior to starting Mavenclad (cladrabine) with live-attenuated or live vaccines given at least 4-6 weeks prior to starting Mavenclad (cladrabine)

7. Anti-herpes prophylaxis is used in an individual with lymphocyte count < 200 cell per microliter

8. There are **NO** contraindications
   - Contraindications include:
     - Individual with current malignancy

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- Woman who is pregnant
- Woman of reproductive potential who does not plan to use effective contraception
- Man of reproductive potential who does not plan to use effective contraception
- Individual with HIV
- Use in an individual with chronic active infections (e.g., hepatitis or tuberculosis)
- Woman who is breast feeding an infant or child

9. Individual does not have moderate to severe renal impairment (CrCl < 60 mL/min)

10. Individual does not have moderate to severe hepatic impairment (Child-Pugh score > 6)

11. Will not be used concurrently with other oral multiple sclerosis medications (except for Ampyra (dalfampridine), which is intended to improve walking speed rather than disease progression) or injectable therapies for multiple sclerosis or other immunomodulatory, immuosuppressive or myelosuppressive therapy

12. There are no significant interacting drugs

Initial approval duration:

- **First Treatment Course with two treatment cycles** (**approve at 1.75mg/kg to be administered in two cycles)**
  - Cycle dosage is weight based using 1 or 2 tabs once daily over 4 or 5 days, do not use more than 2 tabs daily

Note: Second Treatment Course is given at least 43 weeks after the last dose of the First Treatment Course/Second Cycle and **must fulfill criteria as listed below**

The safety and efficacy of reinitiating Mavenclad (cladrabine) more than 2 years after completing 2 Treatment Courses has not been studied

- **Criteria for continuation of coverage (renewal request):** Mavenclad (cladrabine) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a physician specializing in Neurology or is in consultation with a Neurologist

2. Individual successfully completed First Treatment Course

3. Individual has been adherent with the medication

4. Second Treatment Course to begin at least 43 weeks after the last dose of the First Treatment Course/Second Cycle

5. **ALL** of the required tests as listed in the **criteria for initial therapy** section have been completed before initiation of **EACH** treatment course with continued monitoring as clinically appropriate

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6. Anti-herpes prophylaxis is used in an individual with lymphocyte count < 200 cell per microliter
7. There are **NO** contraindications as listed in the **Criteria for initial therapy** section
8. Individual does not have moderate to severe renal impairment (CrCl < 60 mL/min)
9. Individual does not have moderate to severe hepatic impairment (Child-Pugh score > 6)
10. Will not be used concurrently with other oral multiple sclerosis medications (except for Ampyra (dalfampridine), which is intended to improve walking speed rather than disease progression) or injectable therapies for multiple sclerosis or other immunomodulatory, immuosuppressive or myelosuppressive therapy
11. There are no significant interacting drugs

Renewal duration:

- One Treatment Course with two treatment cycles
- Second cycle is separated by 23-27 days of the last dose of a first cycle
- Cycle dosage is weight based using 1 or 2 tabs once daily over 4 or 5 days, do not use more than 2 tabs daily
- The safety and efficacy of reinitiating Mavenclad (cladrabine) more than 2 years after completing 2 Treatment Courses has not been studied
- More than 2 Treatment Courses per lifetime **will not** be approved

- Mavenclad (cladrabine) for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome, and
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Treatment with dosing or frequency outside the FDA-approved dosing and frequency

MAVENCLAD® (cladrabine) oral tablet (cont.)

Description:

Mavenclad (cladrabine) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, use of Mavenclad (cladrabine) is recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS. Mavenclad (cladrabine) is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.

It is given as two treatment courses, with two treatment cycles per course. The second treatment course is given at least 43 weeks after the last dose of the first course/second cycle. Each cycle is separated by 23-27 days after the last dose of a cycle. Following the administration of 2 treatment courses, do not administer additional Mavenclad (cladrabine) treatment during the next 2 years. Treatment during these 2 years may further increase the risk of malignancy. The safety and efficacy of reinitiating Mavenclad (cladrabine) more than 2 years after completing 2 treatment courses has not been studied.

Mavenclad (cladrabine) is a nucleoside metabolic inhibitor. The mechanism by which cladribine exerts its therapeutic effects in patients with multiple sclerosis has not been fully elucidated but is thought to involve cytotoxic effects on B and T lymphocytes through impairment of DNA synthesis, resulting in depletion of lymphocytes. Cladribine is a prodrug that becomes active upon phosphorylation to its 2-chlorodeoxyadenosine triphosphate (Cd-ATP) metabolite.

Resources:

Mavenclad (cladrabine)product information accessed 04-15-19 at DailyMed:
https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9c75e30a-a410-40f1-b653-04d532bd9144

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.