# Mavenclad (cladribine)
# Policy Number: C17329-A

**CRITERIA EFFECTIVE DATES:**

| ORIGINAL EFFECTIVE DATE | LAST REVIEWED DATE | NEXT REVIEW DATE |
|---|---|---|
| 6/1/2019 | 2/12/2020 | 2/12/2021 |
| **J CODE** | **TYPE OF CRITERIA** | **LAST P&T APPROVAL/VERSION** |
| J8499 (NOC) | RxPA | Q2 2020 20200422C17329-A |

**PRODUCTS AFFECTED:**
Mavenclad (cladribine)

**DRUG CLASS:**
Multiple Sclerosis Agents - Antimetabolites

**ROUTE OF ADMINISTRATION:**
Oral

**PLACE OF SERVICE:**
Specialty Pharmacy

**AVAILABLE DOSAGE FORMS**:
Mavenclad (4 Tabs) TBPK 10MG, Mavenclad (5 Tabs) TBPK 10MG, Mavenclad (6 Tabs) TBPK 10MG, Mavenclad (7 Tabs) TBPK 10MG, Mavenclad (8 Tabs) TBPK 10MG, Mavenclad (9 Tabs) TBPK 10MG, Mavenclad (10 Tabs) TBPK 10MG

**FDA-APPROVED USES:**
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 is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS

*Limitations of Use:* MAVENCLAD is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile

**COMPENDIAL APPROVED OFF-LABELED USES:**
None

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**COVERAGE CRITERIA: INITIAL AUTHORIZATION**

**DIAGNOSIS:**
Relapsing forms of multiple sclerosis (MS)

**REQUIRED MEDICAL INFORMATION:**
A. RELAPSING FORMS OR ACTIVE SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS :

1. Documentation of a definitive diagnosis of a relapsing form of multiple sclerosis as defined by the McDonald criteria(see Appendix), including: Relapsing-remitting multiple sclerosis [RRMS], OR secondary-progressive multiple sclerosis [SPMS]
   AND

2. Member is not currently being treated with another disease modifying agent (DMA other than the requested agent)
   AND
3. Prescriber attests that member does not have a concurrent malignancy/cancer
   AND
4. Documentation member has completed the following:, complete blood count (CBC), Varicella zoster vaccination or titers and recent LFT completed
   AND
5. Prescriber attests that member is not pregnant AND if woman is of childbearing potential, confirmation she is using reliable contraception and has been counseled on the risks of this therapy with pregnancy
   AND
6. Prescriber attests that member is not HIV positive (labeled contraindication HIV infection)
   AND
7. Prescriber attests that member does not have any ACTIVE chronic infection (i.e. hepatitis or tuberculosis)
8. Documentation of recent (within last 6 months) of bodyweight for dosing
   AND
9. Prescriber attests that if a woman intends on breastfeeding during Mavenclad (cladribine) therapy, she has been counseled of the contraindication and the appropriate waiting period
   AND
10. Documentation of **inadequate response (trial of 3 months) to EACH of the following:
    (a) ONE of Interferon therapy (Avonex, Rebif, Extavia, Betaseron, Plegridy) OR Glatiramer OR Aubagio (teriflunomide) OR Tecfidera (dimethyl fumerate)
    AND
    (b) ONE of the following: Tysabri (natalizumab) OR Ocrevus (ocrelizumab) OR Gilenya (fingolimod)
    **Inadequate response is defined as meeting at least TWO (2) of the following three criteria during treatment: 1) Clinical relapses (at least two relapses within the past 12 months), 2) CNS lesions progression as measured by MRI, OR 3) Worsening disability (e.g. sustained worsening of EDSS score or neurological exam findings; worsening disability include, but not limited to, decreased mobility, decreased ability to perform activities of daily living due to disease progression, or EDSS > 3.5)

**DURATION OF APPROVAL:**
Initial authorization: 12 months (2 cycles per course, 1 course per year), Continuation of therapy: 12 months (2 cycles per course, 1 course per year). MAXIMUM OF 2 COURSES (2 YEARS) PER LIFETIME. Re-initiation of therapy after four years has not been studied AND will not be approved

**QUANTITY:**
Quantity is limited to the exact number of tablets needed per body weight for each treatment course
40kg- <50kg: First Cycle- 40mg (4 tabs), Second Cycle-40mg (4 tabs)
50kg- <60kg: First Cycle- 50mg (5 tabs), Second Cycle-50mg (5 tabs)
60kg- <70kg: First Cycle- 60mg (6 tabs), Second Cycle-60mg (6 tabs)
70kg- <80kg: First Cycle- 70mg (7 tabs), Second Cycle-70mg (7 tabs)
80kg- <90kg: First Cycle- 80mg (8 tabs), Second Cycle-70mg (7 tabs)
90kg- <100kg: First Cycle- 90mg (9 tabs), Second Cycle-80mg (8 tabs)
100g- <110kg: First Cycle- 100mg (10 tabs), Second Cycle-90mg (9 tabs)
110kg: First Cycle- 100mg (10 tabs), Second Cycle-100mg (10 tabs)

**PRESCRIBER REQUIREMENTS:**
Prescribed by or in consultation with a board certified neurologist or a multiple sclerosis specialist. Please submit consultation notes if prescribed after consultation

**AGE RESTRICTIONS:**
18 years of age and older

**CONTINUATION OF THERAPY:**
A. RELAPSING FORM OF MULTIPLE SCLEROSIS OR ACTIVE SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS:

1. (a) Documentation of a stable number or decrease in acute attacks (relapses) within the last 6 months
   OR
   (b) Documentation of lack of progression or sustained disability
   OR
   (c) Recent (within last 6 months) MRI shows lack of development of new asymptomatic lesions
   AND
2. Documentation member has been adherent to therapy at least 85% of the time as verified by Prescriber and member's medication fill history
   AND
3. Member has not experienced any intolerable adverse effects or drug toxicity

**CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:**
All other uses of Mavenclad (cladribine) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. History of hypersensitivity to cladribine; Diagnosis of clinically isolated syndrome (CIS); Active chronic infections (e.g., hepatitis or tuberculosis); Presence of current malignancy; HIV infection or active chronic infection (e.g. hepatitis or tuberculosis); Concurrent use with other MS disease modifying agents; Given concurrently with live vaccines; Pregnant women, and women and men of reproductive potential who do not plan to use effective contraception during Mavenclad dosing and for 6 months after the last dose in each treatment course; breastfeeding (during treatment or for 10 days after last dose)

**OTHER SPECIAL CONSIDERATIONS:**
Boxed warning(s):
Malignancy: Treatment with cladribine may increase the risk of malignancy. Cladribine is contraindicated in patients with current malignancy. In patients with prior malignancy or with increased risk of malignancy, evaluate the benefits and risks of the use of cladribine on an individual patient basis. Follow standard cancer screening guidelines in patients treated with cladribine.
Risk of Teratogenicity: Cladribine is contraindicated for use in pregnant women and in women and men of reproductive potential who do not plan to use effective contraception because of the potential for fetal harm. Malformations and embryolethality occurred in animals. Exclude pregnancy before the start of treatment with cladribine in females of reproductive potential. Advise females and males of reproductive potential to use effective contraception during cladribine dosing and for 6 months after the last dose in each treatment course. Stop cladribine if the patient becomes pregnant

**BACKGROUND:**
Multiple Sclerosis (MS)
MS is a chronic, inflammatory, autoimmune disease of the central nervous system that disrupts communications between the brain and other parts of the body. Most people experience their first symptoms of MS between the ages of 20 and 40 years of age. MS is among the most common causes of neurological disability in young adults and occurs more frequently in women than in men. MS is the most common immune-mediated inflammatory demyelinating disease of the central nervous system. MS is characterized pathologically by multifocal areas of demyelination with loss of oligodendrocytes and astroglial scarring. Axonal injury is also a prominent pathologic feature, especially in the later stages. Certain clinical features are typical of MS, but the disease has a highly variable pace and

many atypical forms. For most people, MS starts with a relapsing-remitting course, in which episodes of worsening function (relapses) are followed by recovery periods (remissions). These remissions may not be complete and may leave patients with some degree of residual disability. Many, but not all, patients with MS experience some degree of persistent disability that gradually worsens over time. In some patients, disability may progress independent of relapses, a process termed secondary progressive multiple sclerosis (SPMS). In the first few years of this process, many patients continue to experience relapses, a phase of the disease described as active SPMS. Active SPMS is one of the relapsing forms of MS, and drugs approved for the treatment of relapsing forms of MS can be used to treat active SPMS. MS Unites4 On average, up to 80% of patients with RRMS – the most common form of MS at diagnosis – will develop SPMS. SPMS is a form of MS characterized by progressive and irreversible neurological disability. Most patients transition from RRMS to SPMS over time, which can vary if a patient is on disease modifying drug treatment or not.

RRMS – the most common disease course – is characterized by clearly defined attacks of new or increasing neurologic symptoms. These attacks – also called relapses or exacerbations – are followed by periods of partial or complete recovery (remissions). During remissions, all symptoms may disappear, or some symptoms may continue and become permanent. However, there is no apparent progression of the disease during the periods of remission. At different points in time, RRMS can be further characterized as either active (with relapses and/or evidence of new MRI activity) or not active, as well as worsening (a confirmed increase in disability over a specified period of time following a relapse) or not worsening. An increase in disability is confirmed when the person exhibits the same level of disability at the next scheduled neurological evaluation, typically 6 to 12 months later.
Mavenclad is a purine analog that targets lymphocytes and selectively suppresses the immune system by targeting B and T-lymphocytes. It helps in rapid reduction of natural killer cells with minimal impact on neutrophils, platelets and monocytes.

Efficacy
The efficacy of Mavenclad was shown in a clinical trial called CLARITY (Cladribine Tablets Treating Multiple Sclerosis Orally) which studied 1,326 patients with relapsing forms of MS who had least one relapse in the previous 12 months. The primary outcome of CLARITY was the annualized relapse rate (ARR). Additional outcome measures included the proportion of patients with confirmed disability progression, the time to first qualifying relapse, the mean number of MRI T1 Gadolinium-enhancing (Gd+) lesions, and new or enlarging MRI T2 hyperintense lesions. Disability progression was measured in terms of a 3-month sustained change in expanded disability status scale (EDSS) score of at least one point, if baseline EDSS score was between 0.5 and 4.5 inclusively, at least 1.5 points if the baseline EDSS score was 0, or at least 0.5 point if the baseline EDSS score was at least 5, over a period of at least 3 months.
Mavenclad 3.5 mg/kg resulted in a 58% relative reduction in annualized relapse rate over placebo, with 81% patients having no relapses compared to 63% placebo patients.

Adverse Effects

Per the FDA, Mavenclad must be dispensed with a patient Medication Guide that describes information about the drug's uses and risks. Mavenclad has a Boxed Warning for an increased risk of malignancy and fetal harm. Mavenclad should be stopped if the patient becomes pregnant.
Other warnings include the risk of decreased lymphocyte (white blood cell) counts; lymphocyte counts should be monitored before, during and after treatment. Mavenclad may increase the risk of infections; health care professionals should screen patients for infections, and treatment with Mavenclad should be delayed if necessary. Mavenclad may cause hematologic toxicity and bone marrow suppression, so health care professionals should measure a patient's complete blood counts before, during and after therapy. The drug has been associated with graft-versus-host-disease following blood transfusions with non-irradiated blood. Mavenclad may cause liver injury and treatment should be interrupted or discontinued, as appropriate, if clinically significant liver injury is suspected. The most common (>20%) adverse reactions reported by patients receiving Mavenclad include upper respiratory tract infection, headache, and decreased lymphocyte counts. Serious adverse reactions reported in the clinical program included malignancies (0.27 events per 100 patient years) in Mavenclad treated arms, compared to placebo patients (0.13 events per 100 patient-years), herpes zoster infections (2.0% vs. 0.2%), and oral herpes (2.6% vs. 1.2%).

**APPENDIX:**
Summary of 2017 McDonald Criteria for the Diagnosis of MS

| CLINICAL PRESENTATION | ADDITIONAL CRITERIA TO MAKE MS DIAGNOSIS |
|---|---|
| **...in a person who has experienced a typical attack/CIS at onset** | |
| • 2 or more attacks and clinical evidence of 2 or more lesions; OR<br>• 2 or more attacks and clinical evidence of 1 lesion with clear historical evidence of prior attack involving lesion in different location | None. DIS and DIT have been met. |
| • 2 or more attacks and clinical evidence of 1 lesion | DIS shown by <u>one</u> of these criteria:<br>- additional clinical attack implicating different CNS site<br>- 1 or more MS-typical T2 lesions in 2 or more areas of CNS: periventricular, cortical, juxtacortical, infratentorial or spinal cord |
| • 1 attack and clinical evidence of 2 or more lesions | DIT shown by <u>one</u> of these criteria:<br>- Additional clinical attack<br>- Simultaneous presence of both enhancing and non-enhancing MS-typical MRI lesions, or new T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan)<br>- CSF oligoclonal bands |
| • 1 attack and clinical evidence of 1 lesion | DIS shown by <u>one</u> of these criteria:<br>- Additional attack implicating different CNS site<br>- 1 or more MS-typical T2 lesions in 2 or more areas of CNS: periventricular, cortical, juxtacortical, infratentorial or spinal cord<br>**AND**<br>DIT shown by <u>one</u> of these criteria:<br>- additional clinical attack<br>- Simultaneous presence of both enhancing and non-enhancing MS-typical MRI lesions, or new T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan)<br>- CSF oligoclonal bands |
| **...in a person who has steady progression of disease since onset** | |
| 1 year of disease progression (retrospective or prospective) | DIS shown by at least <u>two</u> of these criteria:<br>- 1 or more MS-typical T2 lesions (periventricular, cortical, juxtacortical or infratentorial)<br>- 2 or more T2 spinal cord lesions<br>- CSF oligoclonal bands |

**DIT** = Dissemination in time **CNS** = central nervous system **CSF** = cerebrospinal fluid
**DIS** = Dissemination in space **T2 lesion** = hyperintense lesion on T2-weighted MRI

***Documentation Requirements:***

*Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.*

**REFERENCES:**


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