Oscar Clinical Guideline: Mavenclad (cladribine) (PG227, Ver. 2)

Mavenclad (cladribine)

Summary

Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system. It typically presents in young adults (generally diagnosed before 50 years of age) with symptoms such as vision problems, muscle weakness, numbness, and difficulty with balance and coordination. The most common form is relapsing-remitting MS (occurring in about 85% of patients), characterized by acute attacks followed by periods of remission. Treatment goals include reducing relapses, slowing disability progression, and managing symptoms. Disease-modifying therapies (DMTs) are the primary treatment approach and include injectable medications (e.g., interferons, glatiramer acetate), oral medications (e.g, dimethyl fumarate, fingolimod, teriflunomide, etc.), and infusion therapies (e.g., natalizumab, ocrelizumab).

Mavenclad (cladribine) is an oral DMT approved for relapsing forms of MS, including relapsing-remitting MS and active secondary progressive MS. It has a unique mechanism of action, selectively depleting lymphocytes, and is administered in two short annual oral treatment courses. However, due to significant potential risks, including increased chances of malignancy and harm to developing fetuses in pregnant women, it is typically prescribed only when patients have not responded adequately to, or cannot tolerate, other MS treatments. It's important to note that because of these safety concerns, Mavenclad

(cladribine) is not recommended for use in patients with clinically isolated syndrome, which is considered an early stage of MS.

Definitions

"Clinically isolated syndrome" refers to a first episode of neurologic symptoms lasting at least 24 hours caused by inflammation or demyelination in the central nervous system.

"Disease-modifying therapy" is a medication that modifies the course of MS by reducing relapses and slowing disability progression.

"Multiple sclerosis" is a chronic autoimmune disease of the central nervous system characterized by inflammation, demyelination, and neurodegeneration.

"Primary progressive MS" refers to worsening neurologic function from the onset of symptoms, without early relapses or remissions.

"Relapse" is defined as the appearance of new symptoms or the worsening of existing symptoms lasting at least 24 hours in the absence of fever or infection.

"Relapsing-remitting MS" refers to a disease course characterized by clearly defined attacks of new or increasing neurologic symptoms followed by periods of partial or complete recovery.

"Secondary progressive MS" is a disease course following relapsing-remitting MS that is characterized by a progressive worsening of neurologic function over time with or without relapses.

Medical Necessity Criteria for Initial Authorization

The Plan considers Mavenclad (cladribine) medically necessary when recent (within the last 3 months) clinical chart documentation provided indicates the member meets ALL of the following:

1. Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of multiple sclerosis; *AND*
2. The member is 18 years of age or older; *AND*
3. The member has ONE of the following forms of multiple sclerosis:
    a. relapsing-remitting (RRMS)*; or*
    b. active secondary progressive disease (SPMS); *AND*
4. The member is unable to use, or has tried and failed at least TWO of the following:
    a. An interferon beta product (Avonex, Betaseron, Plegridy, or Rebif)*; and/or*
    b. Dimethyl Fumarate (generic Tecfidera)*; and/or*
    c. Fingolimod (generic Gilenya)*; and/or*
    d. Glatiramer acetate (Copaxone, Glatopa)*; and/or*

e. Teriflunomide (generic Aubagio); *AND*

5. The member does not have any of the following contraindications:
    a. Current malignancy*; or*
    b. HIV infection*; or*
    c. Active chronic infections (e.g., hepatitis, tuberculosis)*; or*
    d. Pregnancy or breastfeeding (on the treatment day and for 10 days after the last dose)*; or*
    e. Woman of childbearing potential or men of reproductive potential who do not plan to use effective contraception during Mavenclad (cladribine) dosing and for at least 6 months after the last dose; *AND*
6. Mavenclad (cladribine) will be used as monotherapy for multiple sclerosis (i.e., member is not using and will not use other disease-modifying MS therapies while on Mavenclad); *AND*
7. Mavenclad (cladribine) is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature (see Appendix, Table 1)
    - *The recommended cumulative dose of Mavenclad is 3.5 mg/kg oral dose, administered as 1.75 mg/kg per treatment course (year). Each treatment course consists of 2 treatment cycles:*
        i. *First cycle: daily dosing for 4 or 5 consecutive days in the first month (to start at any time)*
        ii. *Second cycle: daily dosing for 4 or 5 consecutive days in the second month (between 23-27 days after the last dose of the first course/first cycle).*
    - *Maximum of 20 tablets per treatment course (maximum of 10 tablets per cycle).*

<u>If the above prior authorization criteria are met, the requested medication will be authorized for one treatment course (maximum of 20 tablets over 2 cycles in 1 year).</u>

Medical Necessity Criteria for Reauthorization

Reauthorization for a second treatment course[⇅] will be granted if the member has recent (within the last 6-months) clinical documentation showing BOTH of the following:

1. The requested medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; *AND*
2. The member has experienced at least ONE of the following:
    - Improvement in at least ONE objective measure, such as:
        i. Reduced disease activity on MRI*; and/or*
        ii. Improved or stable disability scores*; and/or*
        iii. Reduced relapse rate*; and/or*
        iv. Improved fatigue or walking assessments; *AND/OR*
    - Member has shown stabilization or improvement in at least ONE MS symptom, such as:
        i. Motor function*; and/or*

ii. Fatigue*; and/or*
iii. Vision*; and/or*
iv. Bowel/bladder function*; and/or*
v. Spasticity*; and/or*
vi. Walking/gait*; and/or*
vii. Pain/numbness/tingling; *AND*

3. At least 43 weeks have passed since the last dose of Mavenclad; *AND*
4. Lymphocyte count is at least 800 cells/μL.
5. Mavenclad (cladribine) is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature (see Appendix, Table 1)
    - *The recommended cumulative dose of Mavenclad is 3.5 mg/kg oral dose, administered as 1.75 mg/kg per treatment course (year). Each treatment course consists of 2 treatment cycles:*
        i. *First cycle: daily dosing for 4 or 5 consecutive days in the first month (to start at any time).*
        ii. *Second cycle: daily dosing for 4 or 5 consecutive days in the second month (between 23-27 days after the last dose of the first course/first cycle).*
    - *Maximum of 20 tablets per treatment course (maximum of 10 tablets per cycle).*
    - *Maximum of 40 tablets over 2 years (four treatment cycles).*

NOTE: The Plan does not consider treatment with Mavenclad (cladribine) beyond two courses (i.e., beyond a cumulative dose of 3.5 mg/kg annually for 2 years) to be medically necessary. The safety and efficacy of additional courses have not been established in clinical trials, and the FDA-approved labeling does not provide guidance for extended use. The drug's mechanism of action results in sustained efficacy beyond the administration period. Continued treatment may increase risks, particularly of malignancy, without clear evidence of additional clinical benefit. Given these factors and the availability of alternative MS therapies, the Plan will not authorize Mavenclad use beyond two treatment courses. Members experiencing disease activity after completing two courses should discuss alternative treatment options with their healthcare provider.

Experimental or Investigational / Not Medically Necessary

Mavenclad (cladribine) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Treatment courses beyond two years .
- Use for the treatment of clinically isolated syndrome (CIS).
- Use for the treatment of primary progressive multiple sclerosis (PPMS).

- Use in combination with other disease-modifying therapies for MS.
- Use in members with current malignancy.
- Use in members with HIV infection.
- Use in pediatric members (under 18 years of age).
- Use in pregnant or breastfeeding women.
- Use for the treatment of myasthenia gravis, Mavenclad (cladribine) is currently being studied in a phase III study for the indication of myasthenia gravis and pending FDA approval.

Appendix

Table 1: Mavenclad (cladribine) Manufacturer Dose Recommendation Per Cycle by Patient Weight in Each Treatment Course

Weight Range	Dose in mg (Number of 10 mg Tablets) per Cycle	
Kilograms (kg)	First Cycle	Second Cycle
40* to less than 50	40 mg (4 tablets)	40 mg (4 tablets)
50 to less than 60	50 mg (5 tablets)	50 mg (5 tablets)
60 to less than 70	60 mg (6 tablets)	60 mg (6 tablets)
70 to less than 80	70 mg (7 tablets)	70 mg (7 tablets)
80 to less than 90	80 mg (8 tablets)	80 mg (8 tablets)
90 to less than 100	90 mg (9 tablets)	90 mg (9 tablets)
100 to less than 110	100 mg (10 tablets)	100 mg (10 tablets)
110 and above	100 mg (10 tablets)	100 mg (10 tablets)
**The use of Mavenclad (cladribine) in patients weighing less than 40 kg has not been investigated.*		

The recommended cumulative dosage of Mavenclad (cladribine) is 3.5 mg/kg body weight administered orally and divided into 2 yearly treatment courses (1.75 mg/kg per treatment course) (see Table 1 above). Each treatment course is divided into 2 treatment cycles:

Administration of First Treatment Course

- First Course/First Cycle: start any time.
- First Course/Second Cycle: administer 23 to 27 days after the last dose of First Course/First Cycle.

Administration of Second Treatment Course

- Second Course/First Cycle: Administer at least 43 weeks after the last dose of First Course/Second Cycle.

Second Course/Second Cycle: administer 23 to 27 days after the last dose of Second Course/First Cycle.

Administer the cycle dosage as 1 or 2 tablets once daily over 4 or 5 consecutive days. Do not administer more than 2 tablets daily.

Following the administration of 2 treatment courses, do not administer additional Mavenclad (cladribine) 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 (cladribine) more than 2 years after completing 2 treatment courses has not been studied.

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