Oscar Clinical Guideline: Mavenclad (cladribine) (PG227, Ver. 1)

Mavenclad (cladribine)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system. It typically presents in young adults with symptoms such as vision problems, muscle weakness, numbness, and difficulty with balance and coordination. The most common form is relapsing-remitting MS, 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 (interferons, glatiramer acetate), oral medications (dimethyl fumarate, fingolimod, teriflunomide, etc.), and infusion therapies (natalizumab, ocrelizumab).

Mavenclad (cladribine) is an oral DMT approved for relapsing forms of MS, including RRMS and active SPMS. It has a unique mechanism of action, selectively depleting lymphocytes, and is administered in two short annual treatment courses. However, due to significant potential risks, including increased chances of malignancy and harm to developing fetuses, it is typically prescribed only when patients have

not responded adequately to other MS treatments or cannot tolerate them. It's important to note that because of these safety concerns, 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. Is 18 years of age or older; ***AND***
3. Has **ONE** of the following forms of multiple sclerosis:
    a. relapsing-remitting (RRMS)***; or***

b. active secondary progressive disease (SPMS); ***AND***

4. 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. 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***; or***
    e. Woman of childbearing potential or man who do not plan to use effective contraception during Mavenclad 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.
    - *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.*
        ii. *Second cycle: daily dosing for 4 or 5 consecutive days in the second month.*
    - *Maximum of 10 tablets per treatment course.*
    - *Maximum of 20 tablets over 2 years.*

If the above prior authorization criteria are met, the requested medication will be authorized for one treatment course (maximum of 10 tablets over 2 cycles in 1 year).

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:

a. 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***
b. 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.

⇅***NOTE:*** *The Plan does not consider treatment with Mavenclad (cladribine) beyond two courses (i.e., beyond a cumulative dose of 3.5 mg/kg over 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 (cumulative dose exceeding 3.5 mg/kg).
- Treatment of clinically isolated syndrome (CIS).
- 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.

References

1. Bainbridge JL, Miravalle A, Wong PS. Multiple Sclerosis. In DiPiro JT, Yee GC, Posey LM, et al, eds. Pharmacotherapy: A Pathophysiologic Approach. 11th ed. New York, NY: McGraw-Hill; 2019.
2. Bartosik-Psujek H, Kaczyński Ł, Górecka M. Cladribine tablets versus other disease-modifying oral drugs in achieving no evidence of disease activity (NEDA) in multiple sclerosis-A systematic review and network meta-analysis.. Mult Scler Relat Disord. 2021; 49:102769.
3. Comi G, Cook S, Rammohan K et al. Long-term effects of cladribine tablets on MRI activity outcomes in patients with relapsing-remitting multiple sclerosis: the CLARITY Extension study. Ther Adv Neurol Disord. 2018; 11:1756285617753365.
4. Deeks ED. Cladribine Tablets: A Review in Relapsing MS. CNS Drugs. 2018; 32:785-796.
5. Giovannoni G, Comi G, Cook S et al. A placebo-controlled trial of oral cladribine for relapsing multiple sclerosis. N Engl J Med. 2010; 362:416-26.
6. Giovannoni G, Soelberg Sorensen P, Cook S et al. Safety and efficacy of cladribine tablets in patients with relapsing-remitting multiple sclerosis: Results from the randomized extension trial of the CLARITY study. Mult Scler. 2018; 24:1594-1604.
7. Hauser, S., & Cree, B. (2020). Treatment of Multiple Sclerosis: A Review.. The American journal of medicine. https://doi.org/10.1016/j.amjmed.2020.05.049.
8. Hermann R, Karlsson MO, Novakovic AM et al. The Clinical Pharmacology of Cladribine Tablets for the Treatment of Relapsing Multiple Sclerosis. Clin Pharmacokinet. 2019; 58:283-297.
9. Mavenclad (cladribine) [prescribing information]. Rockland, MA: EMD Serono Inc; May 2024.
10. McGinley MP, Goldschmidt CH, Rae-Grant AD. Diagnosis and Treatment of Multiple Sclerosis: A Review. JAMA. 2021;325(8):765–779. doi:10.1001/jama.2020.26858
11. Montalban X, Leist TP, Cohen BA et al. Cladribine tablets added to IFN-β in active relapsing MS: The ONWARD study. Neurol Neuroimmunol Neuroinflamm. 2018; 5:e477.
12. Multiple Sclerosis Society of Canada. Disease-modifying therapies. https://mssociety.ca/managing-ms/treatments/medications/disease-modifying-therapies-dmts.
13. National MS Society. Disease-modifying therapies for MS (updated March 2022). Available from National MS Society website: https://nms2cdn.azureedge.net/cmssite/nationalmssociety/media/msnationalfiles/brochures/brochure-the-ms-disease-modifying-medications.pdf.
14. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018;90(17):777-788.
15. Reich DS, Lucchinetti CF, Calabresi PA. 2018. Multiple sclerosis. New England Journal of Medicine 378(2):169-180

16. The use of disease-modifying therapies in multiple sclerosis: principles and current evidence summary. Multiple Sclerosis Coalition. Available from the National MS Society Website: https://www.nationalmssociety.org/.
17. Tramacere I, Del Giovane C, Salanti G, et al. Immunomodulators and immunosuppressants for relapsing-remitting multiple sclerosis: a network meta-analysis. Cochrane Database Syst Rev 2015;9:CD011381.
18. Yang, J., Rempe, T., Whitmire, N., Dunn-Pirio, A., & Graves, J. (2022). Therapeutic Advances in Multiple Sclerosis. Frontiers in Neurology, 13. https://doi.org/10.3389/fneur.2022.824926.

Clinical Guideline Revision / History Information

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