

## Teriflunomide (Aubagio)

### 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 (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 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).

Teriflunomide (Aubagio) is an immunomodulatory agent with disease-modifying properties in multiple sclerosis. Teriflunomide is the active metabolite of leflunomide (a medication used in the treatment of conditions such as rheumatoid arthritis) and works by inhibiting pyrimidine synthesis. It is approved for use in adult patients with relapsing forms of MS, which includes:

1. Clinically isolated syndrome.
2. Relapsing-remitting MS.
3. Active secondary progressive 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 (DMT)" 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 Teriflunomide (Aubagio) 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); *or*
  - c. clinically isolated syndrome (CIS); *AND*
4. For Brand name Aubagio ONLY - member is unable to use, or has tried and failed BOTH of the following:
  - a. generic teriflunomide from at least two different manufacturers; *and*
  - b. at least TWO of the following:
    - i. An interferon beta product (Avonex, Betaseron, Plegridy, or Rebif); *and/or*
    - ii. Dimethyl Fumarate (generic Tecfidera); *and/or*
    - iii. Fingolimod (generic Gilenya); *and/or*
    - iv. Glatiramer acetate (Copaxone); *AND*

5. Teriflunomide (Aubagio) 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 teriflunomide); **AND**
6. Teriflunomide (Aubagio) is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature.
  - o *Teriflunomide 7 mg: 30 tablets per 30 days.*
  - o *Teriflunomide 14 mg: 30 tablets per 30 days.*

If the above prior authorization criteria are met, the requested medication will be authorized for up to 12 months.

#### Medical Necessity Criteria for Reauthorization

Reauthorization for up to 12 months 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. The 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.

#### Experimental or Investigational / Not Medically Necessary

Teriflunomide (Aubagio) 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:

- Use for the treatment of other neurological conditions not related to multiple sclerosis.
- Use for the treatment of primary progressive multiple sclerosis.
- Use in combination with other disease-modifying therapies for multiple sclerosis.

- Use in members under 18 years of age.

## References

1. Aubagio (teriflunomide) [prescribing information]. Cambridge, MA: Genzyme Corporation; June 2024.
2. 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.
3. Confavreux C, O'Connor P, Comi G, et al,. Oral teriflunomide for patients with relapsing multiple sclerosis (TOWER): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Neurol*. 2014 Mar;13(3):247-56. doi: 10.1016/S1474-4422(13)70308-9. Epub 2014 Jan 23.
4. Coyle PK, Khatri B, Edwards KR, et al,. Teriflunomide real-world evidence: Global differences in the phase 4 Teri-PRO study. *Mult Scler Relat Disord*. 2019 Jun;31:157-164. doi: 10.1016/j.msard.2019.03.022. Epub 2019 Mar 30.
5. Freedman MS, Wolinsky JS, Wamil B, et al,. Teriflunomide added to interferon- $\beta$  in relapsing multiple sclerosis: a randomized phase II trial. *Neurology*. 2012 Jun 5;78(23):1877-85. doi: 10.1212/WNL.0b013e318258f7d4. Epub 2012 May 23.  
Hauser SL, Cree BAC. Treatment of Multiple Sclerosis: A Review. *Am J Med*. 2020 Dec;133(12):1380-1390.e2. doi: 10.1016/j.amjmed.2020.05.049. Epub 2020 Jul 17
6. Lebrun-Frénay C, Siva A, Sormani MP, et al. Teriflunomide and Time to Clinical Multiple Sclerosis in Patients With Radiologically Isolated Syndrome: The TERIS Randomized Clinical Trial. *JAMA Neurol*. 2023 Oct 1;80(10):1080-1088. doi: 10.1001/jamaneurol.2023.2815.
7. 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
8. Miller AE, Macdonell R, Comi G, et al,. Teriflunomide reduces relapses with sequelae and relapses leading to hospitalizations: results from the TOWER study. *J Neurol*. 2014 Sep;261(9):1781-8. doi: 10.1007/s00415-014-7395-7. Epub 2014 Jun 28.
9. Miller AE, Olsson TP, Wolinsky JS, et al,. Long-term safety and efficacy of teriflunomide in patients with relapsing multiple sclerosis: Results from the TOWER extension study. *Mult Scler Relat Disord*. 2020 Nov;46:102438. doi: 10.1016/j.msard.2020.102438. Epub 2020 Aug 1.
10. Miller AE, Wolinsky JS, Kappos L, et al,. Oral teriflunomide for patients with a first clinical episode suggestive of multiple sclerosis (TOPIC): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Neurol*. 2014 Oct;13(10):977-86. doi: 10.1016/S1474-4422(14)70191-7. Epub 2014 Sep 2.
11. Montalban X, Gold R, Thompson AJ, et al.ECTRIMS/EAN guideline on the pharmacological treatment of people with multiple sclerosis [published correction appears in *Eur J Neurol*. 2018;25(3):605]. *Eur J Neurol*. 2018;25(2):215-237. doi:10.1111/ene.13536.
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. O'Connor P, Comi G, Freedman MS, et al,. Long-term safety and efficacy of teriflunomide: Nine-year follow-up of the randomized TEMSO study. *Neurology*. 2016 Mar 8;86(10):920-30. doi: 10.1212/WNL.0000000000002441. Epub 2016 Feb 10. Erratum in: *Neurology*. 2016 Oct 4;87(14):1524. doi: 10.1212/WNL.0000000000003219.
15. O'Connor P, Wolinsky JS, Confavreux C, et al. Randomized trial of oral teriflunomide for relapsing multiple sclerosis. *N Engl J Med*. 2011;365(14):1293-1303.

16. 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.
17. Reich DS, Lucchinetti CF, Calabresi PA. 2018. Multiple sclerosis. *New England Journal of Medicine* 378(2):169-180
18. 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/>.
19. 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.
20. Vermersch P, Czlonskowska A, Grimaldi LM, et al., Teriflunomide versus subcutaneous interferon beta-1a in patients with relapsing multiple sclerosis: a randomised, controlled phase 3 trial. *Mult Scler*. 2014 May;20(6):705-16. doi: 10.1177/1352458513507821. Epub 2013 Oct 14.
21. 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

Original Date: 06/27/2024

Reviewed/Revised: 10/01/2025