

Clinical Policy: Teriflunomide (Aubagio)

Reference Number: CP.PHAR.262

Effective Date: 08.01.16

Last Review Date: 05.24

Line of Business: Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Teriflunomide (Aubagio[®]) is a pyrimidine synthesis inhibitor.

FDA Approved Indication(s)

Aubagio is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that teriflunomide and Aubagio are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Sclerosis (must meet all):

1. Diagnosis of one of the following (a, b, or c):
 - a. Clinically isolated syndrome;
 - b. Relapsing-remitting MS, and failure of **generic dimethyl fumarate** at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
 - c. Secondary progressive MS;
2. Prescribed by or in consultation with a neurologist;
3. Age \geq 18 years;
4. For brand Aubagio requests, member must use **generic teriflunomide**, unless contraindicated or clinically significant adverse effects are experienced;
5. Aubagio is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
6. Documentation of both baseline number of relapses per year and expanded disability status scale (EDSS) score;
7. At the time of request, member is not receiving leflunomide;
8. Dose does not exceed the following (a and b):
 - a. 14 mg per day;
 - b. 1 tablet per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Multiple Sclerosis (must meet all):

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member meets one of the following (a or b):
 - a. If member has received < 1 year of total treatment: Member is responding positively to therapy;
 - b. If member has received \geq 1 year of total treatment: Member meets one of the following (i, ii, iii, or iv):
 - i. Member has not had an increase in the number of relapses per year compared to baseline;
 - ii. Member has not had \geq 2 new MRI-detected lesions;
 - iii. Member has not had an increase in EDSS score from baseline;
 - iv. Medical justification supports that member is responding positively to therapy;
3. Aubagio is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
4. For brand Aubagio requests, member must use **generic teriflunomide**, unless contraindicated or clinically significant adverse effects are experienced;
5. If request is for a dose increase, new dose does not exceed the following (a and b):
 - a. 14 mg per day;
 - b. 1 tablet per day.

Approval duration:

If member has received < 1 year of total treatment – up to a total of 12 months of treatment

If member has received \geq 1 year of total treatment – 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 for Medicaid or evidence of coverage documents;
- B. Primary progressive MS.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

EDSS: expanded disability status scale
 FDA: Food and Drug Administration
 MS: multiple sclerosis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
dimethyl fumarate (Tecfidera [®])	<u>Initial:</u> 120 mg PO BID for 7 days <u>Maintenance:</u> 240 mg PO BID	480 mg/day

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): severe hepatic impairment; pregnancy or females of reproductive potential not using effective contraception; hypersensitivity to teriflunomide, leflunomide or any inactive ingredients in Aubagio; current leflunomide treatment
- Boxed warning(s): hepatotoxicity, embryofetal toxicity

Appendix D: General Information

- Disease-modifying therapies for MS are: glatiramer acetate (Copaxone[®], Glatopa[®]), interferon beta-1a (Avonex[®], Rebif[®]), interferon beta-1b (Betaseron[®], Extavia[®]), peginterferon beta-1a (Plegridy[®]), dimethyl fumarate (Tecfidera[®]), diroximel fumarate (Vumerity[®]), monomethyl fumarate (Bafiertam[™]), fingolimod (Gilenya[®], Tascenso ODT[™]), teriflunomide (Aubagio[®]), alemtuzumab (Lemtrada[®]), mitoxantrone (Novantrone[®]), natalizumab (Tysabri[®], and biosimilar Tyruko[®]), ocrelizumab (Ocrevus[®]), cladribine (Mavenclad[®]), siponimod (Mayzent[®]), ozanimod (Zeposia[®]), ponesimod (Ponvory[™]), ublituximab-xiyy (Briumvi[™]), and ofatumumab (Kesimpta[®]).
- Teriflunomide is the principal active metabolite of leflunomide and is responsible for leflunomide's activity in vivo. At recommended doses, teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Relapsing MS	7 or 14 mg PO QD with or without food	14 mg/day

VI. Product Availability

Tablets: 7 mg, 14 mg

VII. References

1. Aubagio Prescribing Information. Cambridge, MA: Genzyme Corporation; December 2022. Available at <https://products.sanofi.us/aubagio/aubagio.pdf>. Accessed January 12, 2024.
2. 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. Full guideline available at: <https://www.aan.com/Guidelines/home/GetGuidelineContent/904>. Reaffirmed on September 18, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review: no significant changes; added Commercial and HIM lines of business (CP.PCH.02 retired); modified Commercial approval durations from Length of Benefit to 6/12 months; references reviewed and updated.	01.27.20	05.20
Added requirements for documentation of baseline relapses/EDSS and objective measures of positive response upon re-authorization; modified continued approval duration to 6 months for the first re-authorization and 12 months for second/subsequent re-authorizations; references reviewed and updated.	05.27.20	08.20
Per November SDC and prior clinical guidance, removed Commercial and HIM LOB from policy (CP.PCH.40 created); added requirement for trial of generic dimethyl fumarate for Medicaid LOB.	11.11.20	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Per November SDC and prior clinical guidance, modified to reflect that trial of generic dimethyl fumarate applies only to RRMS.	02.09.21	
2Q 2021 annual review: no significant changes; updated Appendix C with revised boxed warning per FDA label; references reviewed and updated.	02.10.21	05.21
2Q 2022 annual review: no significant changes; references reviewed and updated.	02.07.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.13.22	
Per SDC, added redirection to generic teriflunomide for brand Aubagio requests.	04.03.23	
2Q 2023 annual review: no significant changes; to be inclusive of members continuing therapy from a different benefit, revised continued approval duration to reference the duration of total treatment received rather than the number of re-authorizations; references reviewed and updated.	01.30.23	05.23
2Q 2024 annual review: no significant changes; revised policy/criteria section to also include generic teriflunomide; references reviewed and updated.	01.25.24	05.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to

applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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