Clinical Policy: Teriflunomide (Aubagio)

Reference Number: CP.PHAR.262
Effective Date: 08.01.16
Last Review Date: 05.19
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 patients with relapsing forms of multiple sclerosis (MS).

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 Aubagio is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Sclerosis (must meet all)**:**

1. Diagnosis of relapsing-remitting MS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Failure of one of the following (a or b) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced:
   a. Avonex® or Plegridy® and any of the following: glatiramer (*generic [including Glatopa®] is preferred*), Tecfidera®, Gilenya™;
   b. Any 2 of the following agents: glatiramer acetate (*generic [including Glatopa®] is preferred*), Tecfidera, Gilenya;

   **Prior authorization is required for all disease modifying therapies for MS*
5. Aubagio is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
6. At the time of request, member is not receiving leflunomide;
7. Dose does not exceed 14 mg (1 tablet) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Multiple Sclerosis (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Aubagio is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
4. If request is for a dose increase, new dose does not exceed 14 mg (1 tablet) per day.

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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
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
Avonex®, Rebif® (interferon beta-1a)	*Avonex*: 30 mcg IM Q week *Rebif*: 22 mcg or 44 mcg SC TIW	*Avonex*: 30 mcg/week *Rebif*: 44 mcg TIW
Plegridy® (peginterferon beta-1a)	125 mcg SC Q2 weeks	125 mcg/2 weeks
Betaseron®, Extavia® (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
glatiramer acetate (Copaxone®, Glatopa®)	20 mg SC QD or 40 mg SC TIW	20 mg/day or 40 mg TIW
Gilenya™ (fingolimod)	0.5 mg PO QD	0.5 mg/day
Tecfidera® (dimethyl fumarate)	120 mg PO BID for 7 days, followed by 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): hepatoxocity, risk of teratogenicity

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®), fingolimod (Gilenya™), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), and ocreliuzmab (Ocrevus™).
- 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; November 2016. Available at http://www.aubagio.com. Accessed February 4, 2019.
2. Costello K, Halper J, Kalb R, Skutnik L, Rapp R. The use of disease-modifying therapies in multiple sclerosis, principles and current evidence – a consensus paper by the Multiple Sclerosis Coalition. March 2017. Accessed February 4, 2019.
3. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.18 MS Treatments. Criteria: added max dosing, clarified monotherapy restriction, removed re-authorization requirement for documented adherence, updated contraindications and reasons to discontinue, modified efficacy criteria to “Responding positively to therapy”. Modified renewal approval duration to 12	06.16	08.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
months. Requirement for the trial and failure of at least 2 preferred regimens from different classes added. Removed specific strength requirement from glatiramer.		
Added age requirement. Removed MRI requirement. Removed hypersensitivity reaction and active infection contraindications. Removed reasons to discontinue.	07.17	08.17
2Q 2018 annual review: no significant changes; removed severe hepatic impairment as a contraindication per safety guidance endorsed by Centene Medical Affairs; references reviewed and updated.	01.05.18	05.18
2Q 2019 annual review: no significant changes; specified that generic forms of glatiramer are preferred; references reviewed and updated.	02.04.19	05.19

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.