Clinical Policy Title:	teriflunomide
Policy Number:	RxA.018
Drug(s) Applied:	Aubagio®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Teriflunomide is a pyrimidine synthesis inhibitor indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
teriflunomide (Aubagio®)	Relapsing MS	7 or 14 mg PO once daily with or without food	14 mg/day

Dosage Forms

- Tablet: 7 mg, 14 mg

Clinical Policy

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

I. Initial Approval Criteria

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

1. Member has a diagnosis of relapsing-remitting MS, which includes clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease;
2. Prescribed by or in consultation with a neurologist;
3. Member is 18 years of age or older;
4. Teriflunomide is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
5. At the time of request, member is not receiving leflunomide;
6. Dose does not exceed 14 mg (1 tablet) per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy (e.g., reduction in MS relapse rate);
3. Teriflunomide 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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MS: Multiple Sclerosis

APPENDIX B: Therapeutic Alternatives
Not applicable

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 teriflunomide; and
  - Coadministration with leflunomide.

- Boxed Warning(s):
  - Hepatoxocity: Clinically significant and potentially life-threatening liver injury, including acute liver failure requiring transplant, has been reported. Concomitant use of teriflunomide with other hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of teriflunomide and monitor ALT levels at least monthly for six months. If drug induced liver injury is suspected, discontinue teriflunomide and start accelerated elimination procedure.
  - Embryofetal toxicity: Teratogenicity and embryolethality occurred in animals administered teriflunomide. Exclude pregnancy prior to initiating teriflunomide therapy. Advise use of effective contraception in females of reproductive potential during treatment and during an accelerated drug elimination procedure. Stop teriflunomide and use an accelerated drug elimination procedure if the patient becomes pregnant.

APPENDIX D: General Information

- 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.
- Disease-modifying therapies for MS include:
  - Infusion therapies
    - natalizumab (Tysabri®)

        - mitoxantrone (Novantrone®)
        - ocrelizumab (Ocrevus™)
        - alemtuzumab (Lemtrada®)
        - rituximab (Rituxan®) (off-label)
    - Injectable therapies
        - glatiramer (Copaxone®, Glatopa®)
        - interferon beta-1a (Avonex®, Rebif®)
        - interferon beta-1b (Betaseron®, Extavia®)
        - ofatumumab (Kesimpta®)
        - peginterferon beta-1a (Plegridy®)
    - Oral therapies
        - cladribine (Mavenclad®)
        - dalfampridine (Ampyra®)
        - dimethyl fumarate (Tecfidera®)
        - diroximel fumarate (Vumerity®)
        - fingolimod (Gilenya™)
        - monomethyl fumarate (Bafiertam™)
        - ozanimod (Zeposia®)
        - siponimod (Mayzent®)
        - teriflunomide (Aubagio®)

References

1. Aubagio Prescribing Information. Cambridge, MA: Genzyme Corporation; November 2020. Available at http://www.aubagio.com. Accessed February 1, 2021.
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 1, 2021.
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. Accessed February 1, 2021.
4. Teriflunomide. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI; 2020, November 12. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed January 20, 2021.
5. Olek, M.J. & Mowry, E. Initial disease-modifying therapy for relapsing-remitting multiple sclerosis in adults. In: UpToDate, Gonzalez-Scarano, F. & Dashe, J.F. (Eds), UpToDate, Waltham, MA; 2020, December 15. Accessed with subscription at: www.uptodate.com. Accessed February 1, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy reviewed and updated: 1. Indication updated to be more specific 2. References	5/2020	5/20/2020
Policy reviewed and updated: 1. Clinical policy title & lines of business updated. 2. Initial criteria for approval and duration updated. 3. Continued therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance…". 4. Appendix D updated. 5. References updated.	02/01/2021	03/09/2021