teriflunomide (Aubagio®, generics)

Policy # 00758
Original Effective Date: 01/01/2022
Current Effective Date: 11/11/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider teriflunomide (Aubagio®, generics)‡ for the treatment of relapsing forms of multiple sclerosis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for teriflunomide (Aubagio, generics) will be considered when the following criteria are met:

- Patient has a relapsing form of multiple sclerosis (including clinically isolated syndrome, relapsing-remitting disease, active secondary progressive disease); AND
- If the request is for brand Aubagio, patient has tried and failed (e.g., intolerance or inadequate response) GENERIC teriflunomide unless there is clinical evidence or patient history that suggests generic teriflunomide will be ineffective or cause an adverse reaction to the patient. *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of brand Aubagio when the patient has not tried and failed GENERIC teriflunomide to be **not medically necessary.****

teriflunomide (Aubagio®, generics)

Policy # 00758
Original Effective Date: 01/01/2022
Current Effective Date: 11/11/2024

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of teriflunomide (Aubagio, generics) when the patient selection criteria are not met (except that denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Aubagio is indicated for the treatment of relapsing forms of multiple sclerosis and works by inhibiting dihydroorotate dehydrogenase and pyrimidine synthesis to reduce the number of activated lymphocytes in the central nervous system (CNS). It was one of the first approved oral therapies for multiple sclerosis and should be administered as either 7 mg or 14 mg by mouth once daily. Because it is associated with hepatotoxicity, embryofetal toxicity, immunosuppression, and increased blood pressure; several monitoring requirements exist prior to treatment initiation. Patients should have liver function tests and a complete blood count within 6 months before initiation of Aubagio and be screened for latent tuberculosis infection. Additionally, pregnancy should be excluded prior to initiation in females of reproductive potential and blood pressure should be monitored in all patients before the start of Aubagio treatment and periodically thereafter.

Multiple sclerosis (MS) is believed to have an immunologic mechanism that is characterized by demyelination in the brain and spinal cord. This is often expressed by symptoms such as visual and oculomotor abnormalities, weakness, urinary dysfunction, and mild cognitive impairment. In the most common forms of MS, patients experience remissions and exacerbations. Treatment includes corticosteroids for acute exacerbations and immunomodulatory (disease modifying) drugs to prevent exacerbations. Disease modifying drugs include oral products such as fingolimod (Gilenya®)‡, ponesimod (Ponvory™)‡, siponimod (Mayzent®)‡, ozanimod (Zeposia®)‡, dimethyl fumarate (Tecfidera®, generics)‡, diroximel fumarate (Vumerity®)‡, teriflunomide (Aubagio), and cladribine (Mavenclad®)‡; subcutaneous and intramuscular injectable products such as glatiramer acetate (Copaxone®, generics)‡, interferon beta-1a (Avonex®, Rebif®)‡, interferon beta-1b (Extavia®, Betaseron®)‡, peginterferon beta-1a (Plegridy®)‡, and ofatumumab (Kesimpta®)‡; and intravenous infusions such as ocrelizumab (Ocrevus®)‡, natalizumab (Tysabri®)‡, and alemtuzumab (Lemtrada®)‡.

teriflunomide (Aubagio®, generics)

Policy # 00758
Original Effective Date: 01/01/2022
Current Effective Date: 11/11/2024

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Aubagio is approved for the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Aubagio was established in four randomized, controlled, double-blind clinical trials in patients with relapsing forms of multiple sclerosis.

Study 1 was a double-blind, placebo-controlled clinical trial that evaluated once daily doses of Aubagio 7 mg and Aubagio 14 mg for up to 26 months in patients with relapsing forms of multiple sclerosis. Patients were required to have a diagnosis of multiple sclerosis exhibiting a relapsing clinical course, with or without progression, and to have experienced at least one relapse over the year preceding the trial or at least two relapses over the two years preceding the trial. Patients were required not to have received any multiple sclerosis medication for at least six months before entering the study and these medications were not permitted during the study. Neurological evaluations were performed at screening, every 12 weeks until week 108, and after suspected relapses. The primary endpoint was the annualized relapse rate (ARR). In this study, 1088 patients were randomized to receive Aubagio 7 mg (n=366), Aubagio 14 mg (n=359), or placebo (n=363). The ARR was found to be 0.37 in the Aubagio 7 mg group, 0.369 in the Aubagio 14 mg group, and 0.539 in the placebo group. Both Aubagio groups had ARRs that were statistically significantly reduced compared to the placebo (p=0.0002 and 0.0005, respectively).

Study 2 was a double-blind, placebo-controlled clinical trial that evaluated once daily doses of Aubagio 7 mg and Aubagio 14 mg for up to 40 months in patients with relapsing forms of multiple sclerosis. Patients were required to have a diagnosis of multiple sclerosis exhibiting a relapsing clinical course and to have experienced at least one relapse over the year preceding the trial, or at

least two relapses over the two years preceding the trial. Patients were required to not have received any multiple sclerosis medication for at least three months before entering the trial, nor were these medications permitted during the trial. Neurological evaluations were to be performed at screening, every 12 weeks until completion, and after every suspected relapse. The primary endpoint was the ARR. A total of 1165 patients received Aubagio 7 mg (n=407), Aubagio 14 mg (n=370), or placebo (n=388). The ARR was found to be 0.389 in the Aubagio 7 mg group, 0.319 in the Aubagio 14 mg group, and 0.501 in the placebo group. Both Aubagio groups had ARRs that were statistically significantly reduced compared to placebo (p=0.0183 and 0.0001, respectively).

Study 3 was a double-blind, placebo-controlled clinical trial that evaluated once daily doses of Aubagio 7 mg and Aubagio 14 mg for up to 108 weeks in patients with relapsing multiple sclerosis. Patients were required to have had a first clinical event consistent with acute demyelination occurring within 90 days of randomization with 2 or more T2 lesions at least 3 mm in diameter that were characteristic of multiple sclerosis. A total of 614 patients received Aubagio 7 mg (n=203), Aubagio 14 mg (n=214), or placebo (n=197). The proportion of patients free of relapse was greater in the Aubagio 8mg (70.5%, p<0.05) and Aubagio 14 mg (72.2%, p<0.05) groups than in the placebo group (61.7%).

The effect of Aubagio on MRI activity was also demonstrated in Study 4, a randomized, double-blind, placebo-controlled clinical trial of multiple sclerosis patients with relapse. In this study, MRI was to be performed at baseline, 6 weeks, 12 weeks, 18 weeks, 24 weeks, 30 weeks, and 36 weeks after treatment initiation. A total of 179 patients were randomized to Aubagio 7 mg (n=61), Aubagio 14 mg (n=57), or placebo (n=61). Baseline demographics were consistent across treatment groups. The primary endpoint was the average number of unique active lesions/MRI scan during treatment. The mean number of unique active lesions per brain MRI scan during the 36-week treatment period was lower in patients treated with Aubagio 7 mg (1.06) and Aubagio 14 mg (0.98) as compared to placebo (2.69). This difference was statistically significant for both (p=0.0234 and p=0.0052, respectively).

References

1. Aubagio [package insert]. Genzyme Corporation. Greenwood Village, Colorado.

teriflunomide (Aubagio®, generics)

Policy # 00758
Original Effective Date: 01/01/2022
Current Effective Date: 11/11/2024

Policy History

Original Effective Date: 01/01/2022
Current Effective Date: 11/11/2024

10/07/2021	Medical Policy Committee review
10/13/2021	Medical Policy Implementation Committee approval. New policy.
10/06/2022	Medical Policy Committee review
10/11/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/05/2023	Medical Policy Committee review
10/11/2023	Medical Policy Implementation Committee approval. Title changed from "teriflunomide (Aubagio®)" to "teriflunomide (Aubagio®, generics)". New criterion requiring trial of generic prior to brand added to policy.
10/03/2024	Medical Policy Committee review
10/08/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 10/2025

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);

teriflunomide (Aubagio®, generics)

Policy # 00758
Original Effective Date: 01/01/2022
Current Effective Date: 11/11/2024

2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.