LOUISIANA BLUE

Pharmacotherapy for Geographic Atrophy

Policy # 00850
Original Effective Date: 09/11/2023
Current Effective Date: 01/13/2025

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.

Note: pegcetacoplan (Empaveli™) is addressed separately in medical policy 00768.

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 pegcetacoplan (Syfovre™)‡ or avacincaptad pegol (Izervay™)‡ for the treatment of geographic atrophy to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for pegcetacoplan (Syfovre) or avacincaptad pegol (Izervay) will be considered when the following criteria are met:

- Patient has a diagnosis of geographic atrophy of the macula secondary to dry age-related macular degeneration; AND
- The geographic atrophy lesion area is $\geq$ 2.5 mm^2; AND
  *(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.)*
- Patient does not have a history of or active choroidal neovascularization or wet age-related macular degeneration at the initiation of treatment; AND
  *(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.)*
- Patient does not have any ocular or periocular infections or active intraocular inflammation; AND
- Patient meets ONE of the following:
  - Requested drug is Syfovre and dose will not exceed 15 mg per eye every 25 days; OR
  - Requested drug is Izervay and dose will not exceed 2 mg per eye every 21 days for a maximum duration of 12 months.

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of pegcetacoplan (Syfovre) or avacincaptad pegol (Izervay) when the geographic atrophy lesion is smaller than 2.5 mm^2 or the patient has a history of or active choroidal neovascularization or wet age-related macular degeneration to be **not medically necessary.****

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 pegcetacoplan (Syfovre) or avacincaptad pegol (Izervay) when the patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Syfovre and Izervay are each complement inhibitors approved for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD). Syfovre contains the active ingredient, pegcetacoplan, a complement C3 inhibitor that is the same ingredient in Empaveli™‡, but the indication, dosage form, dose, and route of administration are different than Empaveli. Both drugs work by blocking C3 and downregulating the complement system. For Syfovre, this is thought to decrease the pathogenesis and progression of GA. Syfovre is administered via intravitreal injection to each affected eye once every 25 to 60 days. Izervay is also a complement inhibitor but inhibits complement protein C5. Izervay should be administered via intravitreal injection to each affected eye once monthly for up to 12 months. Clinical trials of both products found an increased incidence of neovascular AMD in the treatment group compared to the sham group, so the FDA labeling suggests monitoring of patients for signs of neovascular AMD. Additionally, patients with ocular history of or active choroidal neovascularization were excluded from the pivotal trials of both drugs.

AMD is a chronic, multifactorial, progressive central retinal disease that is the leading cause of irreversible blindness in the elderly population. It is divided into two types: exudative or neovascular (“wet”) and nonexudative (“dry”). GA is caused by the gradual breakdown of light-sensitive cells in the macula, resulting in the growth of irreversible lesions in the retinal pigment epithelium that can lead to impaired vision or blindness. It has several potential causes, but can be caused by dry AMD (intermediate and advanced stages of disease). At this time, there are no other medical therapies for GA.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Syfovre was approved in February 2023 for the treatment of geographic atrophy secondary to age-related macular degeneration.

Izervay was approved in August 2023 for the treatment of geographic atrophy secondary to age-related macular degeneration.

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.

Syfovre

The safety and efficacy of Syfovre were assessed in two multi-center, randomized, sham-controlled studies (OAKS and DERBY) in patients with GA (atrophic nonexudative age-related macular degeneration), with or without subfoveal involvement, secondary to AMD in a total of 1258 randomized patients. Both studies were 24 months in duration with patients randomly assigned in a 2:2:1:1 ratio to 1 of 4 dosing regimens:

1.) Syfovre administered at 15 mg/0.1 mL monthly;
2.) Syfovre administered at 15 mg/0.1 mL every other month;
3.) Sham administered monthly;
4.) Sham administered every other month.

In OAKS, 31% of patients in the monthly group, 21% of patients in the every other month group, and 25% of patients in the sham groups discontinued treatment prior to Month 24. In DERBY, 29% of patients in the monthly group, 22% of patients in the every other month group, and 21% of the patients in the sham groups discontinued treatment prior to Month 24.

There was a reduction in the mean rate of GA lesion growth observed in both studies. In OAKS, there was a decrease of 0.87 in the slope of the rate of GA lesion growth in the monthly group compared to the pooled sham group (95% CI -1.27 to -0.47) and a decrease of 0.72 in the every other month group compared to the pooled sham group (95% CI -1.10 to -0.33). In DERBY, there was a slope decrease of 0.73 in the monthly Syfovre group compared to the pooled sham group (95% CI: -1.14 to -0.31) and a decrease of 0.70 in the every other month Syfovre group (95% CI: -1.11 to -0.28).

Izervay
The safety and efficacy of Izervay were demonstrated in two randomized, multi-center, double-masked, sham-controlled, 18- and 12-month studies (GATHER1 and GATHER2) in patients with GA due to AMD. Patient ages ranged from 51 to 97 years with a mean of 77 years. In total, 292 patients were treated with Izervay 2 mg, and 332 patients received sham.

In GATHER1 and GATHER2, the mean rate of GA growth (slope) from baseline to Month 12, measured by Fundus Autofluorescence (FAF) was evaluated at 3 time points: baseline, Month 6, and Month 12. Data are available through Month 18 for GATHER1 and Month 12 for GATHER2. At any time during the study, patients that developed choroidal neovascularization were concomitantly treated with anti-VEGF therapy.

In each study, over a 12-month period, there was a statistically significant reduction of the rate of GA growth (0.10 mm/year; $p<0.01$ in GATHER1 and 0.05 mm/year; $p<0.01$ in GATHER2 with square root transformed data) in patients treated with Izervay compared to sham.

References

1. Syfovre [package insert]. Apellis Pharmaceuticals, Inc. Waltham, MA. Updated Feb 2023.
2. Syfovre Drug Evaluation. Express Scripts. Updated March 2023.
3. Izervay [package insert]. Iveric bio, Inc. Northbrook, IL. Updated Dec 2023.

Policy History

Original Effective Date: 09/11/2023
Current Effective Date: 01/13/2025

08/03/2023	Medical Policy Committee review
08/09/2023	Medical Policy Implementation Committee approval. New policy.
09/19/2023	Coding update
02/01/2024	Medical Policy Committee review
02/14/2024	Medical Policy Implementation Committee approval. Added new drug, Izervay to the policy with relevant criteria and background information. Changed title from "pegcetacoplan (Syfovre)" to "Pharmacotherapy for Geographic Atrophy." Changed denial for active ocular inflammation or infection to investigational.
03/26/2024	Coding update
12/05/2024	Medical Policy Committee review
12/11/2024	Medical Policy Implementation Committee approval. Updated criteria to remove upper limit on lesion size and clarify that patients who develop wet AMD while on therapy are still eligible for treatment.

Next Scheduled Review Date: 12/2025

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	67028
HCPCS	J2781, J2782 Delete code effective 10/01/2023: C9151 Delete code effective 04/01/2024: C9162 Delete codes effective 01/01/2025: C9399, J3490
ICD-10 Diagnosis	All related diagnoses

*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);
    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.