

Pharmacotherapy for Geographic Atrophy

Policy # 00850

Original Effective Date: 09/11/2023

Current Effective Date: 05/01/2026

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

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 greater than or equal to 2.5 mm²; 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.

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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 mm² 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 EmpaveliTM†, 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. 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.

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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 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 24-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, patients were treated with either Izervay or sham monthly for 18 months. In the primary analysis for GATHER1, 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. Over a 12-month period, there was a statistically significant reduction of the rate of GA growth (0.10 mm/year; $p < 0.01$ with square root transformed data) in patients treated with Izervay compared to sham.

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In the 24-month GATHER2 study, patients were treated with Izervay or sham monthly for the first 12 months. Patients receiving monthly Izervay were re-randomized at Month 12 to receive either Izervay monthly (EM) or every other month (EOM). Patients treated with sham in the first 12 months continued monthly sham treatment. At any time during the GATHER2 study, patients that developed choroidal neovascularization were concomitantly treated with anti-VEGF therapy.

In GATHER2 analysis, the mean rate of GA growth (slope) measured by FAF was evaluated at 5 time points: baseline, Month 6, Month 12, Month 18, and Month 24. Over a 12-month period, there was a statistically significant reduction of the rate of GA growth (0.05 mm/year; $p < 0.01$ with square root transformed data) in patients treated with Izervay EM compared to sham. The annualized rate of GA growth over 24 months in the monthly arm was 2.23 mm²/year, resulting in treatment difference versus sham of 0.36 mm²/year ($p = 0.0165$). In the treatment arm that included patients who received Izervay EM treatment for one year and EOM treatment for the second year, the annualized rate of GA growth was 2.10 mm²/year.

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 March 2025.

Policy History

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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.
04/03/2025	Medical Policy Committee review
04/09/2025	Medical Policy Implementation Committee approval. Updated Izervay criteria and background information to reflect FDA label expansion allowing for treatment beyond 12 months.
04/02/2026	Medical Policy Committee review
04/10/2026	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 04/2027

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Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2025 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 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);

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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.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.