Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCTOP043.0624	**TOPICAL PRODUCTS** **GEOGRAPHIC ATROPHY AGENTS** **Izervay®** (avacincaptad pegol sodium pf vial) **Syfovre®** (pegcetacoplan-pf vial)
Effective Date: 8/1/2024	**Review/Revised Date**: 11/23, 04/24 (JN)
Original Effective Date: 08/23	**P&T Committee Meeting Date**: 06/23, 12/23, 06/24
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicare Part B
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-Approved Indications

REQUIRED MEDICAL INFORMATION:
For initial authorization, all the following criteria must be met:
1. Documentation of diagnosis of geographic atrophy (GA) confirmed by clinical exam or diagnostic imaging (such as Color Fundus Photography, Fundus Autofluorescence, Near Infrared Reflectance Imaging, Optical Coherence Tomography)
2. Documentation that GA is secondary to age-related macular degeneration (AMD)
3. If active choroidal neovascularization (CNV) present, documentation must be submitted attesting that treatment with the requested medication is medically necessary and appropriate monitoring of CNV will be conducted (such as a comprehensive eye exam within three months of starting the requested therapy)

For reauthorization for Syfovre®, the following must be met: Documentation of response to therapy defined as one of the following:
1. Reduction in GA growth lesion
2. Documentation of improvement in visual function through visual function assessment test (such as normal luminance best-correct visual acuity [BCVA],

maximum reading speed, Functional Reading Independence Index, microperimetry)

For Izervay®, reauthorization will not be allowed.

EXCLUSION CRITERIA:

- Active ocular or periocular infections in the requested eye being treated
- History of endophthalmitis, retinal detachments, or increased intraocular pressure in the requested eye being treated

AGE RESTRICTIONS:

For Iverzay: May be approved for patients aged 50 years and older.
For Syfovre: May be approved for patients aged 60 years and older

PRESCRIBER RESTRICTIONS:

Must be prescribed by, or in consultation with, an ophthalmologist

COVERAGE DURATION:

For Syfovre: Initial authorization and reauthorization will be approved for one year
For Izervay: May be approved for patients aged 50 years and older.

QUANTITY LIMIT:

Izervay:4 mg per 30 days

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:

Pegcetacoplan-pf vial (Syfovre®) is a complement C3 inhibitor and is the first FDA-approved treatment of geographic atrophy (GA) secondary to age-related macular degeneration.

Avacincaptad pegol (Izervay®) is a complement C5 inhibitor indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD). Avacincaptad pegol is the second FDA-approved treatment for geographic GA with an FDA approval for treatment up to 12 months

FDA APPROVED INDICATIONS:
Indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

POSITION STATEMENT:
- GA is an advanced form of AMD affecting more than 5 million people worldwide, including 22% of people over 90 years old. GA is responsible for 10-20% of all incidences of legal blindness caused by AMD. Risk factors for GA include genetic polymorphisms, advanced age (especially over 85 years old), smoking, and presence of early AMD to GA in the fellow eye. Genes that may play a significant role in GA include: Complement Factor H (CFH), Complement Factor B (CFB), Complement 2 (C2), Complement 3 (C3), and ARMS2. Polymorphisms in six complement genes (CFH, CFI, C2/CFB, C3, C9) account for almost 60% of the AMD genetic risk. Symptoms of GA can include scotomas (large dark or blind spots in the visual field), difficulty recognizing faces, decreased reading speed (measured in words per minute, wpm), impaired dark adaptation, low luminance deficit (LLD), impaired contrast sensitivity, and difficulty driving at night.[5]
- Per expert opinion consultation, GA can occur in both wet and dry AMD.
- Most recent guidelines for GA include Age-Related Macular Degeneration Preferred Practice Pattern guideline, published in 2019, which states that at the time there was no proven therapy to prevent or treat GA.[6]
- Pegcetacoplan-pf was approved based off of two phase 3 clinical trials (DERBY and OAKS). The primary endpoint (Change from Baseline to Month 12 in total area of GA lesion[s] in the study eye [in mm2] based on Fundus Autofluorescence [FAF]) was not statistically significant at 12 months in the DERBY trial, but was statistically significant in the OAKS trial at month 12, month 18, and month 24 results as well as in the DERBY trial at month 18 and month 24 results. Reductions in overall GA lesion growth compared to sham injection controlled increased more-so as the months went on. However, at 24 months, there was no statistically significant difference in measures of visual function. Therefore, it is not clear if treatment with Syfovre demonstrated clinically significant results. Inclusion criteria in both trials included age equal or greater to

60 years of age, and clinical diagnosis of GA of the macular secondary to AMD. Exclusion criteria in both trials included GA secondary to a condition other than AMD, any history or active CNV associated with AMD or any other cause, and any contraindication to intravitreal injection including current ocular or periocular infection.

- Safety: Warnings and precautions for Syfovre include endophthalmitis and retinal detachments, neovascular AMD, intraocular inflammation, and increased intraocular pressure. The most common adverse reactions (≥5%) reported in Syfovre clinical trials were ocular discomfort, neovascular age-related macular degeneration (nAMD), vitreous floaters, and conjunctival hemorrhage.
- Avacincaptad pegol (Izervay®) was approved based off two randomized, multi-center, double-masked, sham-controlled trials (GATHER1 and GATHER2). GATHER1 and GATHER2 demonstrated that avacincaptad pegol reduces the GA growth rate over 12 months in patients with GA due to AMD. However, avacincaptad pegol did not have an impact on best corrected visual acuity (BCVA). Patients who completed the second year of GATHER2 will be enrolled in the ongoing open-label extension for an additional 18 months of treatment and safety monitoring for GA secondary to AMD. Therapy duration of avacincaptad pegol (Izervay®) past 12 months will be evaluated once submitted to the FDA after additional research is conducted.

REFERENCE/RESOURCES:

1. Syfovre® package insert. Waltham, MA: Apellis Pharmaceutical, Inc; 2024 March.
2. Syfovre® In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically.
3. Syfovre® In: Lexi-Drugs Online [Internet database]. Hudson, OH: Lexi-Comp, Inc. Updated periodically.
4. Syfovre® (pegcetacoplan-pf) vial Prime Therapeutics Monograph. Updated on March 1, 2023.
5. Geographic atrophy. Pathways and targets for geographic atrophy. Geographic Atrophy (accessed 2023 March 13).
6. Flaxel CJ, Adelman RA, Bailey ST, et al. Age-related macular degeneration preferred practice pattern. *American Academy of Ophthalmology*. 2019;127(1):1-65.
7. Izervay Package insert. Parsippany, NJ. IVERIC bio, Inc. August 9, 2023.
8. Izervay In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically. Accessed November 2, 2023.

9. Izervay In: Lexi-Drugs Online [Internet database]. Hudson, OH: Lexi-Comp, Inc. Updated periodically. Accessed November 2, 2023.
10. Izervay (avacincaptad pegol) vial monograph. Prime Therapeutics. Updated on August 16, 2023.