

LONG-TERM DATA

IZERVAY 3.5-year GATHER2 Open-Label Extension (OLE) Trial: Safety and treatment observations



These OLE analyses help us
better understand IZERVAY's
role in GA management."

– Dr. Arshad M. Khanani, Vitreoretinal Surgeon

INDICATION

IZERVAY® (avacincaptad pegol intravitreal solution) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

IZERVAY is contraindicated in patients with ocular or periocular infections and in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments

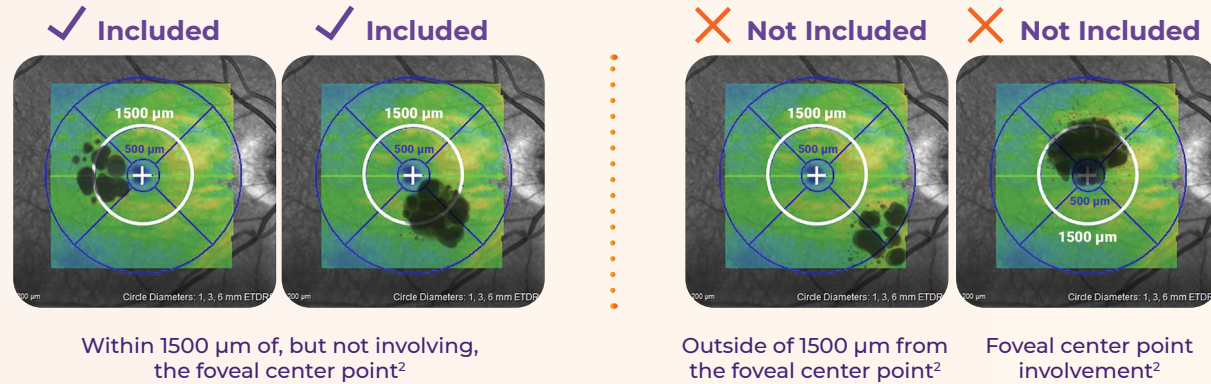
- Intravitreal injections may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.

Please see additional [Important Safety Information](#) on page 9 and full [Prescribing Information](#) for more information.

izervay[®]
(avacincaptad pegol
intravitreal solution) 2 mg

IZERVAY was evaluated in patients with GA secondary to AMD¹

The efficacy and safety of IZERVAY were demonstrated in 2 randomized, multicenter, double-masked, sham-controlled studies in patients with GA due to AMD (GATHER1 and GATHER2).¹



~84% of patients had disease within 500 µm of the foveal center point²

Additional inclusion criteria^{3,4}

- ≥50 years
- BCVA between 20/25 and 20/320
- GA lesions:
 - Total area between 2.5 mm² and 17.5 mm² (1-7 DA, respectively)
 - If multifocal lesions, at least 1 lesion had to be ≥1.25 mm² (0.5 DA)

Additional exclusion criteria^{3,4}

- Evidence of CNV or any sign of diabetic retinopathy in either eye at baseline
- GA secondary to any condition other than AMD in either eye
- Any prior treatment for AMD or any prior intravitreal treatment for any indication in either eye (except oral vitamin or mineral supplements)
- Any ocular condition in study eye that could progress during the study and potentially affect central vision or otherwise act as a confounding factor

Additionally, a Phase 3, open-label, multicenter, 18-month extension study enrolled 278 participants who completed GATHER2 through the Month 24 visit. Unlike the GATHER1 and GATHER2 inclusion criteria, the OLE study allowed participants with center point-involving GA to enroll in the study (32.7% [91/278]).²

DA=disc area; BCVA=best corrected visual acuity; CNV=choroidal neovascularization.

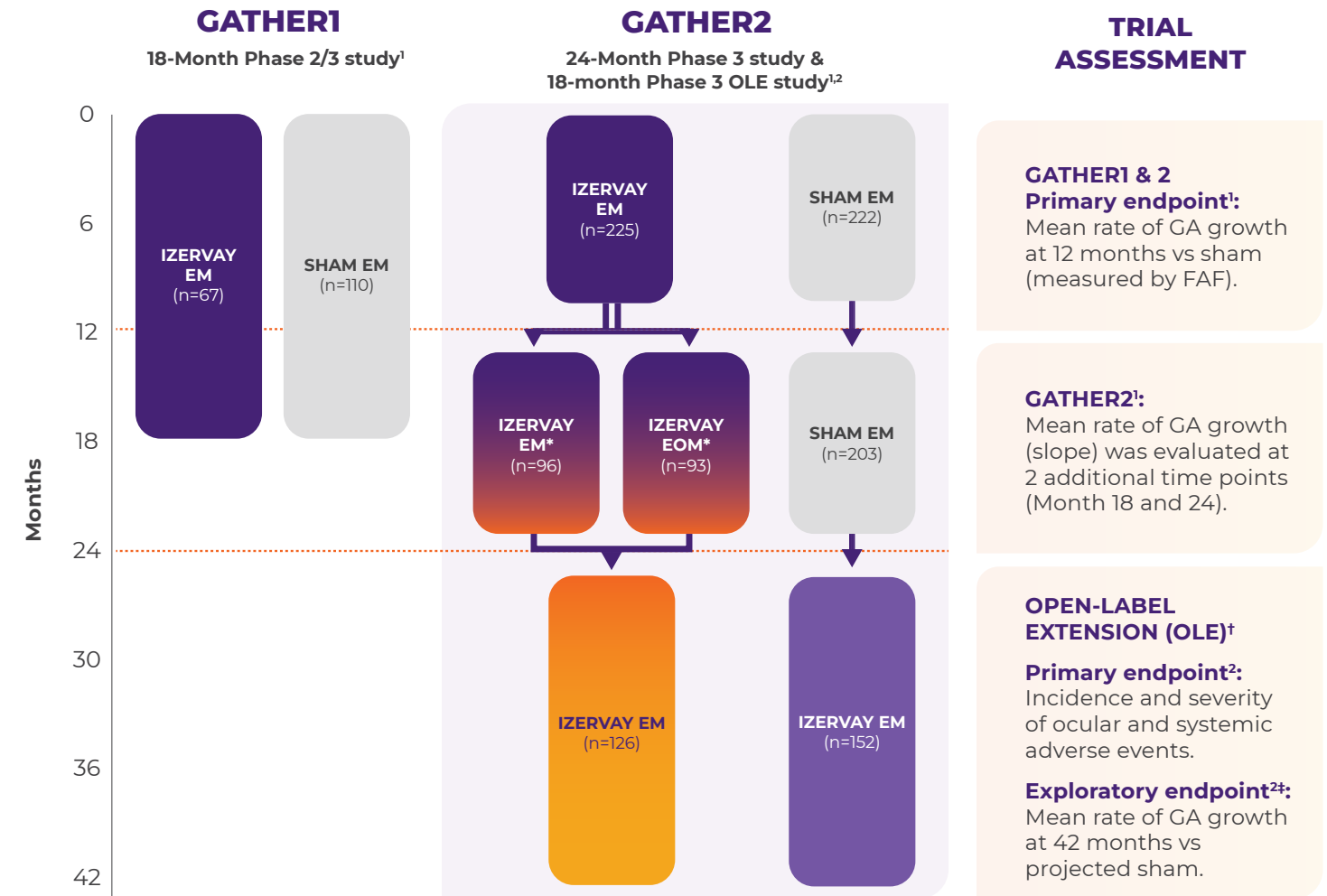
IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Neovascular AMD

- In the GATHER1 and GATHER2 clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Over 24 months, the rate of neovascular (wet) AMD or choroidal neovascularization in the GATHER2 trial was 12% in the IZERVAY group and 9% in the sham group. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.

IZERVAY was assessed in two Phase 3 trials and an open-label extension study through 3.5 years^{1,2}



*Patient re-randomization.

†All participants, regardless of prior GATHER2 treatment (IZERVAY or sham), received IZERVAY in the study eye. All participants were to have a final follow-up visit or follow-up procedure at Month 42 if the study was terminated early. The end of the study was defined as the date of the last study assessment for the last participant in the study globally.

‡Exploratory endpoints include the following ophthalmic variables: BCVA, LLVA, LLD, IOP, OE, and GA area.

The recommended dose for IZERVAY is 2 mg once monthly (approximately 28 +/- 7 days)¹

EM=every month; EOM=every other month; FAF=fundus autofluorescence; IOP=intraocular pressure; LLD=low luminance deficit; LLVA=low luminance visual acuity; OE=ophthalmic examination.

Please see additional **Important Safety Information** on page 9 and full **Prescribing Information** for more information.

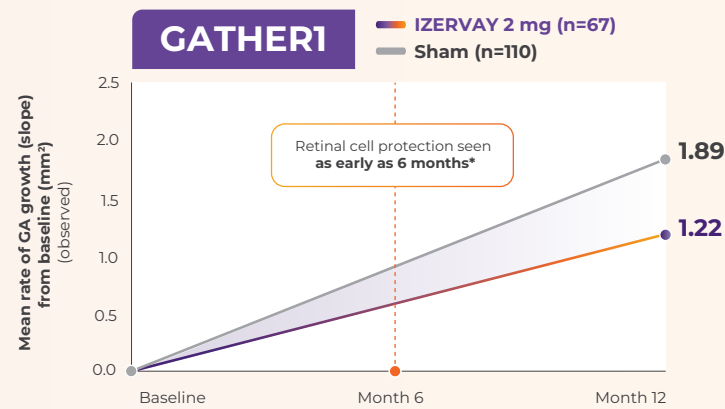
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Primary endpoint data

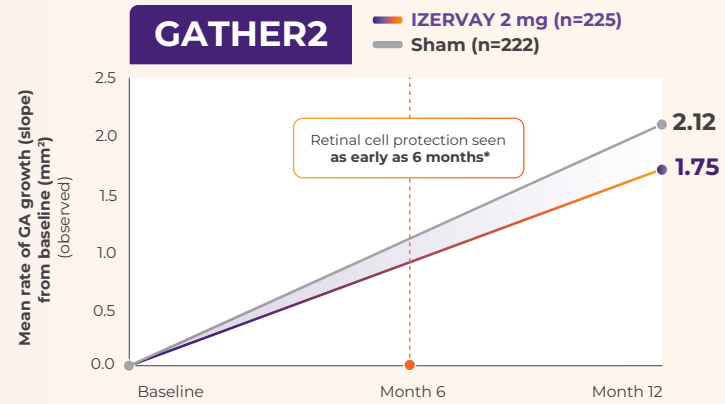
IZERVAY provided significant protection of healthy retinal cells in just one year of treatment¹

The primary endpoint in GATHER1 and 2 evaluated the mean rate of GA growth (slope) from baseline to Month 12, measured by FAF at 3 time points (baseline, Month 6, and Month 12). In GATHER2, the mean rate of GA growth (slope) measured by FAF was evaluated at 2 additional time points (Month 18 and Month 24).¹

Reductions in mean rate of growth (MMRM analysis) at 12 months vs sham¹



35%[†]
REDUCTION AT 12 MONTHS
 Difference in mm²/year: 0.67 (95% CI, 0.21-1.13); p<0.01



18%[†]
REDUCTION AT 12 MONTHS
 Difference in mm²/year: 0.38 (95% CI, 0.12-0.63); p<0.01

IZERVAY is the only GA treatment to demonstrate statistically significant efficacy at one year in two Phase 3 trials^{1,5}

CI=confidence interval; MMRM=mixed models for repeated measures.

*6-month time point was not part of the primary analysis, is observational in nature and should be interpreted with caution, and cannot be considered conclusive.

[†]Percent difference is calculated by 100×(difference)/(least squares mean from sham).

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

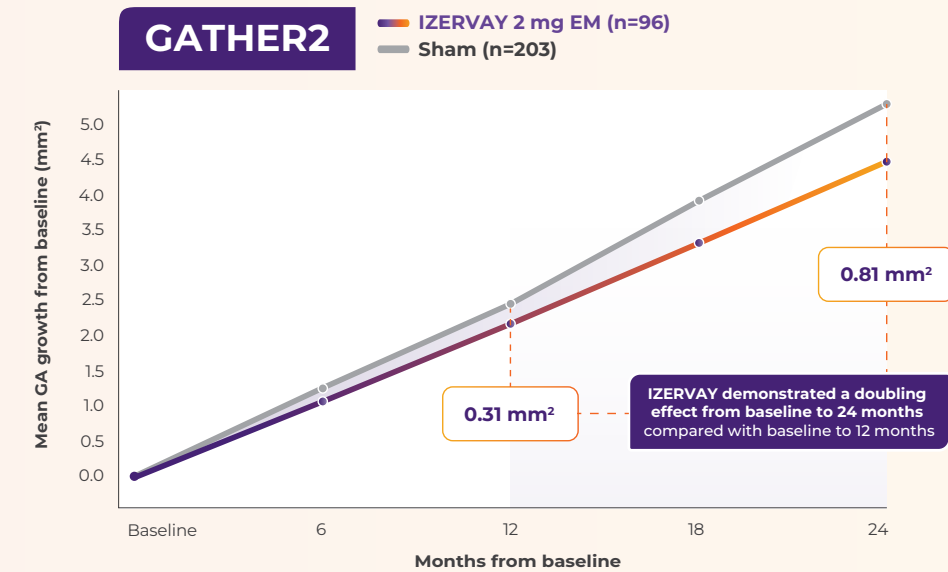
Increase in Intraocular Pressure

- Transient increases in intraocular pressure (IOP) have been observed after an intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

24-Month data

IZERVAY demonstrated an increasing treatment effect over 2 years^{1,6}

Analysis of mean growth in GA area (mm²) at Month 24 vs sham^{2,6‡}



Piecewise spline multivariate slope.

The annualized rate of GA growth (MMRM analysis)[§] at 24 months in GATHER2¹

IZERVAY 2 mg EM

- 2.23 mm²/year
- 14% reduction at 24 months; difference vs sham (95% CI) mm²/year=0.36 (0.07-0.66); p=0.0165^{||}

IZERVAY 2 mg EM to EOM

- 2.10 mm²/year
- Due to the hierarchical testing procedure, no statistical test was performed for the EOM treatment group

The recommended dose for IZERVAY is 2 mg once monthly (approximately 28 +/- 7 days)¹

[‡]Analysis is based on MMRM assuming a piecewise linear trend at Month 6, 12, 18, including effects for treatment, time, and time by treatment interaction.

[§]Non-transformed GA growth slope analysis.

^{||}Percent difference is calculated by 100×(difference)/(least squares mean from sham).

Please see additional Important Safety Information on page 9 and full Prescribing Information for more information.



Safety

**Proven safety through 2 years
in the GATHER trials¹**

IZERVAY is the only FDA-approved GA treatment with no warning and precaution for intraocular inflammation or retinal vasculitis^{1,5}

| Common ocular adverse reactions (≥2%) and greater than sham in study eye ¹ | GATHER1 & GATHER2 12 Months | | GATHER2 24 Months | |
|---|--------------------------------|-----------------|----------------------|-----------------|
| | IZERVAY (n=292) | Sham (n=332) | IZERVAY (n=225) | Sham (n=222) |
| Conjunctival hemorrhage | 13% | 9% | 17% | 9% |
| Increased intraocular pressure (IOP) | 9% | 1% | 13% | 1% |
| Blurred vision* | 8% | 5% | 14% | 5% |
| Choroidal neovascularization (CNV) | 7% | 4% | 12% | 9% |
| Eye pain | 4% | 3% | 7% | 4% |
| Vitreous floaters | 2% | <1% | 4% | <1% |
| Blepharitis | 2% | <1% | 3% | <1% |
| Punctate keratitis [†] | – | – | 10% | 8% |
| Retinal hemorrhage | – | – | 4% | 3% |
| Ocular hypertension | – | – | 4% | 0 |
| Corneal abrasion | – | – | 2% | <1% |

Adverse reactions marked with a dash occurred at a rate of <2% or were not greater than sham at 12 months.

- ≤1% of patients treated with IZERVAY for up to 24 months across the GATHER trials reported experiencing photopsia, ischemic optic neuropathy, vitreous hemorrhage, vitreal cells, vitritis, and endophthalmitis^{1‡}

No cases of retinal vasculitis were reported in the GATHER trials²

**The real-world safety profile across nearly 600k vials of IZERVAY
remains consistent with findings from the GATHER trials^{1,2§}**

*Blurred vision includes visual impairment, vision blurred, visual acuity reduced, visual acuity reduced transiently and blindness transient.
[†]Punctate keratitis includes punctate keratitis and keratitis.
[‡]Culture positive.
[§]As of 02/26. Based on samples and commercially distributed vials.

OLE primary endpoint

**No cases of retinal or occlusive vasculitis
were reported through 3.5 years²**

| Ocular TEAEs ≥2% during open-label extension ² | IZERVAY to IZERVAY EM (n=125) | Sham to IZERVAY EM (n=151) |
|---|----------------------------------|-------------------------------|
| Ocular TEAEs in the study eye, % | 59.2% | 58.3% |
| Increased intraocular pressure (IOP) | 15.2% | 13.2% |
| Cataract | 12.8% | 7.3% |
| Conjunctival hemorrhage | 10.4% | 9.9% |
| Vitreous detachment | 5.6% | 0.7% |
| Visual acuity reduced | 5.6% | 13.2% |
| New-onset CNV | 5.6% | 9.3% |
| Punctate keratitis | 3.2% | 6.0% |
| Transient visual loss | 3.2% | 2.0% |
| Posterior capsule opacification | 2.4% | 4.6% |

IZERVAY treatment duration²:

- IZERVAY to IZERVAY: 42 months
- Sham to IZERVAY: 18 months

TEAE=treatment emergent adverse event.
^{||}New-onset CNV includes patients with CNV incidence during open-label extension portion but not CNV that occurred during the GATHER2 trial.

IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5% and occurred with frequency ≥2% vs. sham) reported in patients receiving IZERVAY for up to 24 months in GATHER2: conjunctival hemorrhage, blurred vision, increased IOP, wet AMD, punctate keratitis, and eye pain.

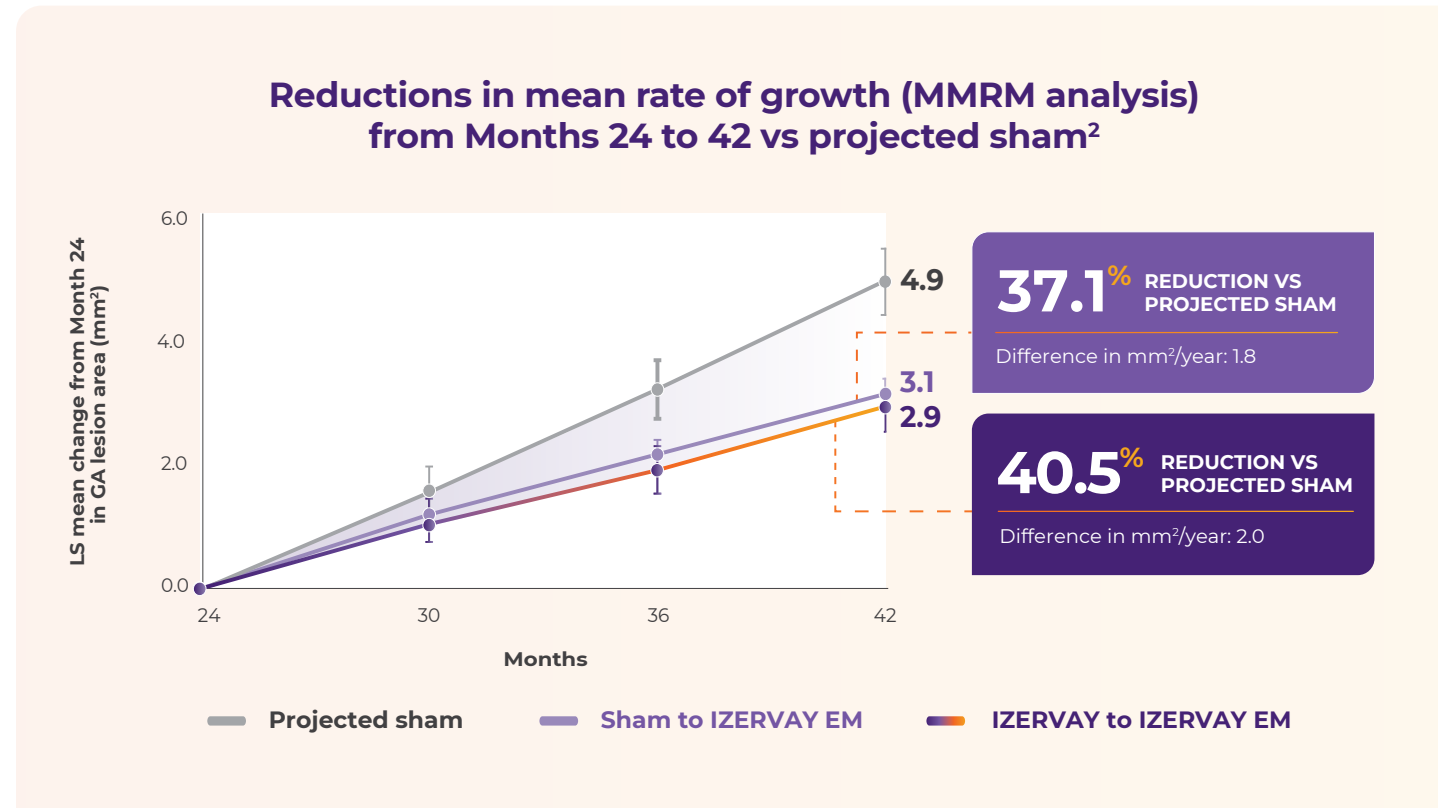
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OLE exploratory endpoint

Observed reduction in rate of GA lesion growth vs projected sham by 37.1% and 40.5% from Months 24-42²

Given the exploratory nature of the data, these results should be interpreted with caution and cannot be considered conclusive. The OLE analysis used a projected sham and may not reflect rate of change for all GA patients. Although prespecified, there was no statistical testing hierarchy. Open-label studies can allow for selection bias; clinical significance is not established.



Methodology: For projected sham, GA growth rate from Month 24 to Month 42 was first calculated as the average transformed growth rates across four 6-month intervals (baseline through Month 24) in the GATHER2 sham group and subsequently converted to the untransformed scale.²

For the IZERVAY groups, a separate piecewise MMRM was applied using square root transformed GA area data. The least squares mean of the square root transformed GA area was calculated and converted to the untransformed scale.²

LS=least squares.

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INDICATION AND IMPORTANT SAFETY INFORMATION

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Physician featured has been compensated.

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Treat to protect with IZERVAY¹

The #1 prescribed FDA-approved treatment for new GA patients^{2*}



Visit [IZERVAYecp.com](https://www.izervayecp.com)
to learn more

*Based on Symphony data from 3/24-12/25. May not represent entire patient population.

References: **1.** IZERVAY. Package insert. Northbrook, IL: Astellas Pharma US, Inc.; 2026. **2.** Astellas Pharma US, Inc. IZERVAY. Data on File. **3.** Patel SS, Lally DR, Hsu J, et al. Avacincaptad pegol for geographic atrophy secondary to age-related macular degeneration: 18-month findings from the GATHER1 trial. *Eye*. 2023;37(17):3551-3557. Erratum in: *Eye*. 2023;37(17):3705. **4.** Khanani AM, Patel SS, Staurengi G, et al. Efficacy and safety of avacincaptad pegol in patients with geographic atrophy (GATHER2): 12-month results from a randomised, double-masked, phase 3 trial. *Lancet*. 2023;402(10411):1449-1458. **5.** Syfovre. Package insert. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2025. **6.** Khanani AM, Danzig CJ, Heier JS, et al. Avacincaptad pegol for geographic atrophy secondary to age-related macular degeneration: 2-year efficacy and safety results from the GATHER2 phase 3 trial [published online ahead of print December 15, 2025]. *Ophthalmology*. 2025. [https://www.aaojournal.org/action/showPdf?pii=S0161-6420\(25\)00790-0](https://www.aaojournal.org/action/showPdf?pii=S0161-6420(25)00790-0).

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