Ophthalmologic Complement Inhibitors (for Ohio Only)

Policy Number: CSOH2024D0118.A
Effective Date: January 1, 2024

Instructions for Use

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Related Policies
None

Application

This Medical Benefit Drug Policy only applies to the state of Ohio. Any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using Ohio Administrative Code 5160-1-01.

Coverage Rationale

Izervay™ and Syfovre® are proven and medically necessary when the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of geographic atrophy (GA) secondary to age-related macular degeneration (AMD); **and**
  - Diagnosis has been confirmed by geographic atrophy secondary to age-related macular degeneration sensitive tests [e.g., optical coherence tomography (OCT), fundus autofluorescence (FAF) imaging]; **and**
  - Macular atrophy is not secondary to any conditions other than AMD (e.g., Stargardt disease, cone rod dystrophy, toxic maculopathies)
  - Prescribed by or in consultation with an ophthalmologist experienced in treatment of retinal diseases; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Authorization is for no more than 12 months.
- For **continuation of therapy**, **all** of the following:
  - Physician attestation that patient would benefit from continued administration; **and**
  - For long term treatment, documentation of titration to the minimum dosing frequency to achieve maximum benefit; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Authorization is for no more than 12 months.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may

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require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
C9399	Unclassified drugs or biologicals
J2781	Injection, pegcetacoplan, intravitreal, 1 mg
J3490	Unclassified drugs
J3590	Unclassified biologics

Diagnosis Code	Description
H35.3113	Nonexudative age-related macular degeneration, right eye, advanced atrophic without subfoveal involvement
H35.3114	Nonexudative age-related macular degeneration, right eye, advanced atrophic with subfoveal involvement
H35.3123	Nonexudative age-related macular degeneration, left eye, advanced atrophic without subfoveal involvement
H35.3124	Nonexudative age-related macular degeneration, left eye, advanced atrophic with subfoveal involvement
H35.3133	Nonexudative age-related macular degeneration, bilateral, advanced atrophic without subfoveal involvement
H35.3134	Nonexudative age-related macular degeneration, bilateral, advanced atrophic with subfoveal involvement

Background

Geographic atrophy (GA) is an advanced form of dry age-related macular degeneration (AMD) caused by destruction of retinal cells through irreversible lesion growth. GA is a progressive disease that typically starts in the prifoveal region and expands to involve the fovea with time, leading to permanent loss of visual acuity. In the United States, GA affects approximately 1 million people, and it is one of the leading causes of blindness.

Lesion growth in geographic atrophy is driven in part by excessive complement activation. Genetic variants of complement C3, play a central role in driving the downstream damaging effects of complement overactivation in the progression of geographic atrophy. Pegcetacoplan is pegylated complement C3 inhibitor peptide that regulates excessive activation of the complement cascade.

Clinical Evidence

Proven

Avacincaptad pegol and pegcetacoplan injection are proven for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

The safety and efficacy of avacincaptad pegol were demonstrated in two randomized, multi-center, double-masked, sham-controlled, 18- and 12-month studies (GATHER1-NCT02686658 and GATHER2-NCT04435366, respectively) 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 avacincaptad pegol 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 GATHER2 study, patients that developed choroidal neovascularization were concomitantly treated with anti-VEGF therapy. In each study, 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 avacincaptad pegol compared to sham. The most common adverse reactions with avacincaptad pegol use were hemorrhage, increased intraocular pressure (IOP), blurred vision, and choroidal neovascularization. The pooled rate of new neovascular (wet) AMD or choroidal neovascularization was 7.0% of patients in the avacincaptad pegol group and 4% in the sham group.

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The efficacy of pegcetacoplan was evaluated in DERBY and OAKS, two Phase 3, randomized, double-masked, sham-controlled studies in 1,258 patients with geographic atrophy secondary to AMD. Patients were randomized to intravitreal injections of pegcetacoplan monthly, pegcetacoplan every other month, or sham. The primary endpoint was the change in total area of geographic atrophy lesion(s) based on fundus autofluorescence imaging at 12 months (p-value < 0.05). Monthly and every-other-month treatment with pegcetacoplan met the primary endpoint in OAKS, significantly reducing GA lesion growth by 22% (p = 0.0003) and 16% (p = 0.0052), respectively, compared to pooled sham at 12 months. DERBY did not meet the primary endpoint, showing a reduction in GA lesion growth of 12% (p = 0.0528) and 11% (p = 0.0750) with monthly and every-other-month treatment, respectively, compared to pooled sham at 12 months. In a prespecified analysis of the combined DERBY and OAKS studies, monthly and every-other-month treatment with pegcetacoplan reduced GA lesion growth by 17% (p < 0.0001) and 14% (p = 0.0012), respectively, compared to pooled sham at 12 months. In a prespecified analysis of the primary endpoint, pegcetacoplan demonstrated a greater effect in patients with extrafoveal lesions at baseline. Patients with GA typically present first with extrafoveal lesions, which then progress toward the fovea where central vision is impacted. In the combined studies, monthly and every-other-month treatment with pegcetacoplan decreased GA lesion growth by 26% (p < 0.0001) and 23% (p = 0.0002), respectively, in patients with extrafoveal lesions compared to pooled sham at 12 months.

Patients in DERBY and OAKS continued to receive masked treatment for 24 months. In a pre-specified analysis, both monthly and every-other-month pegcetacoplan showed a reduction in lesion growth from baseline compared to sham (all p-values are nominal) at month 24: DERBY: 19% monthly (p = 0.0004) and 16% every-other month (p = 0.0030); OAKS: 22% monthly (p < 0.0001) and 18% every-other-month (p = 0.0002).

The pooled rate of new-onset exudations was 6.0% of patients in the monthly pegcetacoplan groups, 4.1% in the every-other-month pegcetacoplan groups, and 2.4% in the sham groups. Two cases of confirmed infectious endophthalmitis and one case of suspected infectious endophthalmitis were observed in the study eye out of a total of 6,331 injections (0.047%). Thirteen events of intraocular inflammation were observed in the studies (0.21% per injection). No events of retinal vasculitis or retinal vein occlusion were observed. There were no clinically relevant changes in vision for patients who developed infectious endophthalmitis or intraocular inflammation.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Avacincaptad pegol and pegcetacoplan injection are indicated in adult patients for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

References

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3. Apellis Pharmaceuticals Press Release. Apellis Pharmaceuticals Web site. Apellis announces FDA acceptance and Priority Review of the New Drug Application for pegcetacoplan for the treatment of geographic atrophy (GA). https://investors.apellis.com/news-releases/news-release-details/apellis-announces-fda-acceptance-and-priority-review-new-drug-0. July 19, 2022. Accessed September 6, 2022.
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6. Patel SS, Lally DR, Hsu J, Wykoff CC, Eichenbaum D, Heier JS, Jaffe GJ, Westby K, Desai D, Zhu L, Khanani AM. Avacincaptad pegol for geographic atrophy secondary to age-related macular degeneration: 18-month findings from the

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GATHER1 trial. Eye (Lond). 2023 Mar 24. doi: 10.1038/s41433-023-02497-w. Epub ahead of print. Erratum in: Eye (Lond). 2023 May 26: PMID: 36964259.

Policy History/Revision Information

Date	Summary of Changes
01/01/2024	• New Medical Benefit Drug Policy

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state (Ohio Administrative Code [OAC]), or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state (OAC), or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state (OAC), or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state (OAC), or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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