February 20, 2025

Stephanie Carlton
CMS Chief of Staff & Acting Administrator
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Sent electronically

RE: Request for Clarification – Recent Claim Denials of Dual Administration for GA and Anti-VEGF

Dear Acting Administrator Carlton,

The American Academy of Ophthalmology (the Academy)[i] and the American Society of Retina Specialists (ASRS)[ii] are writing to seek clarity on recent claim denials for dual administration of geographic atrophy (GA) and anti-vascular endothelial growth factor (anti-VEGF) drugs.

Our organizations have heard from retina specialists that all seven MACs have been denying claims for GA and anti-VEGF drugs when Medicare patients are treated with both types of drugs. The denied claims appear to be for injections of both drugs within 25 days of each other, but the reasoning behind the denials is unclear and our members have received conflicting rationales when appealing the denials. **We are seeking clarification on what recent claim edit or policy changes are resulting in these denials and the rationale behind the denials.**

Age-related macular degeneration (AMD) is a spectrum of macula disorders. GA, a potentially debilitating type of nonexudative AMD (dry AMD), occurs when the retinal pigment epithelium (RPE) and/or choriocapillaris atrophy. Drusen and other pigmentary abnormalities may surround the atrophic areas. Since 2023, the U.S. Food & Drug Administration (FDA) has approved the use of two different complement factor inhibitor drugs (Syfovre and Izervay) for the treatment of GA secondary to Nonexudative AMD. Inhibition of the complement cascade slows growth of GA lesions, which are the primary source of blindness from dry AMD. Syfovre (pegcetacoplan) and Izervay (avacincaptad pegol) are administered by intravitreal injection (CPT 67028, *Intravitreal injection of a pharmacologic agent (separate procedure)*).

Many patients simultaneously have exudative AMD (wet AMD), which their retina specialist may choose to treat with anti-VEGF drug injections. Wet AMD occurs when a neovascular complex originating from the choroid proliferates around the RPE layer of the retina. This can result in hard exudates from vascular leakage, serous and/or hemorrhagic detachment of the neurosensory retina or the RPE, and an elevated, fibrovascular disciform scar.[iii] Anti-VEGF injections target this neovascular proliferation, that when unchecked, is the primary source of blindness from wet AMD. Although more commonly present in isolation, both wet

AMD and GA may coexist in the same eye with both disease forms contributing to visual deterioration via different pathological mechanisms According to the National Eye Institute sponsored study, *Comparison of Age-Related Macular Degeneration Treatments Trials*, the "cumulative incidence [of coexisting GA] was 12% at 1 year, 17% at 2 years, and 38% at 5 years."[iv] While GA was previously untreatable, recent ophthalmic drug innovations have made it possible for different medications to be simultaneously administered to target both conditions. In the DERBY and OAKS studies (two phase 3 trials which culminated in FDA approval of pegcetacoplan), the conversion rate from GA to exudative AMD at 2 years was 12% for every month and 7% for every other month injections. This occasionally required injections of two different medications in the study eye on the same day.[v]

Complement factor inhibitor drugs and anti-VEGF injections are used independently to treat the two distinct disease pathways present in these eyes. Syfovre and Izervay injections lower the immune response to prevent damage to retinal cells, slowing the development of GA.[vi] For wet AMD, anti-VEGF injections reduce the number of abnormal blood vessels in the retina and slow and reverse any leakage from the blood vessels.[vii] For patients with coexisting wet AMD and GA, treatment would necessarily require two injections in the same eye to administer the two different drugs targeting each disease present. Because the frequency of injections required for these two distinct diseases are different, there are cases when an interval of less than 25 days for both injections or even same day injections is required. As an example, a patient may be receiving Syfovre every 8 weeks and Eylea every 6 weeks – yet both are required at this frequency to maintain control of the independent retinal diseases Dry and Wet AMD, respectively.

The dual administration of both complement factor inhibitor drugs and anti-VEGF injections are medically necessary as administered by the patient's retina specialist to treat both GA and exudative AMD occurring simultaneously in the same eye. **Given that the two different diseases are being appropriately treated by retina specialists following FDA-accepted guidance in the package inserts, we respectfully request that CMS instruct the MACs to reverse the claim denials for both complement factor inhibitor drugs and anti-VEGF drugs.**

Our organizations strongly encourage CMS to review and re-evaluate claims processing edits related to intravitreal injections. We would welcome the opportunity to work with CMS and the MACs on developing a revised claim edit.

Retina specialists are experiencing major financial difficulties due to the unpublished edit that is preventing billing GA drugs with anti-VEGF treatments. Edits should be published to the public for review prior to taking effect so that care can be managed prospectively. In addition to our other requests, our organizations are advocating for transparency in changes made to claim edits.

We appreciate CMS' consideration of these concerns and are eager to discuss them in further detail at your convenience. If you have questions or need additional information

regarding any portion of these comments, please contact the Academy's Director of Health Policy, Brandy Keys, MPH, at bkeys@aao.org or via phone at 202-737-6662.

Sincerely,

Michael X. Repka, MD, MBA
President
Medical Director, Governmental Affairs
American Academy of Ophthalmology

John T. McAllister, MD
Secretary for Federal Affairs
American Academy of Ophthalmology

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[i] The American Academy of Ophthalmology is the largest association of eye physicians and surgeons in the United States. A nationwide community of over 20,000 medical doctors, we protect sight and empower lives by setting the standards for ophthalmic education, supporting research, and advocating for our patients and the public.

[ii] ASRS is the largest retina organization in the world, representing over 3,000 board certified ophthalmologists who have completed fellowship training in the medical and surgical treatment of retinal diseases. The mission of the ASRS is to provide a collegial open forum for education, to advance the understanding and treatment of vitreoretinal disease.

[iii] Vemulakonda, G. A., Bailey, S. T., Kim, S. J., Kovach, J. L., Lim, J. I., Ying, G., & Flaxel, C. J. (2025). AAO Preferred Practice pattern®. *Ophthalmology*. https://doi.org/10.1016/j.ophtha.2024.12.018

[iv] Grunwald, J.E., Pistilli, M., Ebenezer, D., Maguire, M.G., & Martin, D.F. (2017). Incidence and Growth of Geographic Atrophy during 5 Years of Comparison of Age-Related Macular Degeneration Treatments Trials. Ophthalmology, 124(1), 97-104. https://doi.org/10.1016/j.ophtha.2016.09.012

[v] Heier, J. S., Lad, E. M., Holz, F. G., Rosenfeld, P. J., Guymer, R. H., Boyer, D., Grossi, F., Baumal, C. R., Korobelnik, J. F., Slakter, J. S., Waheed, N. K., Metlapally, R., Pearce, I., Steinle, N., Francone, A. A., Hu, A., Lally, D. R., Deschatelets, P., Francois, C., Bliss, C., ... OAKS and DERBY study investigators (2023). Pegcetacoplan for the treatment of geographic atrophy secondary to age-related macular degeneration (OAKS and DERBY): two multicentre, randomised, double-masked, shamcontrolled, phase 3 trials. Lancet (London, England), 402(10411), 1434–1448. https://doi.org/10.1016/S0140-6736(23)01520-9

[vi] Mukamal, R. (2024, February 18). *What to know about Syfovre and Izervay for geographic atrophy*. American Academy of Ophthalmology. https://www.aao.org/eye-health/tips-prevention/syfovre-izervay-geographic-atrophy-amd-macular-deg

[vii] Boyd, K. (2024, October 1). *Understanding macular degeneration*. American Academy of Ophthalmology. https://www.aao.org/eye-health/diseases/amd-macular-degeneration