AIMED ALLIANCE

July 2, 2021

Dow Briggs, M.D.
Executive Vice President
BlueCross BlueShield of Alabama
dbriggs@bcbsal.org

Darrel Weaver, M.D.
Vice President of Healthcare Networks Services
BlueCross BlueShield of Alabama
dweaver@bcbsal.org

Anne Schmidt, M.D.
Senior Medical Director
BlueCross BlueShield of Alabama
aschmidt@bcbsal.org

Dear Dr. Briggs, Dr. Weaver, and Dr. Schmidt:

Aimed Alliance is a non-profit health policy organization that works to protect and enhance the rights of health care consumers and providers. Blue Cross Blue Shield of Alabama (BCBS AL) has adopted a new prior authorization policy, effective July 1, 2021, for aflibercept.[1] The policy requires patients with neovascular (wet) age-related macular degeneration (Wet AMD), macular edema following retinal vein occlusion (MEfRVO), diabetic macular edema (DME), and diabetic retinopathy (DR) to try and fail on an off-label, compounded medication before accessing aflibercept, which is FDA approved for such conditions. If a medication to treat these eye conditions is ineffective, patients can experience rapid and severe loss of central vision.[2] Therefore, we recommend that BCBS AL amend its prior authorization policy to remove the step therapy requirements for patients with Wet AMD, MEfRVO, DME, and DR.

I. Background

Macular edema occurs when there is abnormal leakage and accumulation of fluid in the macula from damaged blood vessels in the nearby retina.[3] A common cause of macular edema is diabetic retinopathy, a disease that can happen to people with diabetes.[4] Diabetic retinopathy usually affects both eyes and is the most common diabetic eye disease and the leading cause of irreversible blindness in working age Americans.[5]

Another cause of macular edema is age related macular degeneration. AMD is a progressive eye disease that blurs the central vision due the deterioration or breakdown of the

[1] https://al-policies.exploremyplan.com/portal/web/medical-policies/-/ph-90026?print=1
[2] https://visionaware.org/your-eye-condition/age-related-macular-degeneration-amd/treatments-for-wet-macular-degeneration/#:~:text=In%20wet%20(neovascular%2Fexudative),severe%20loss%20of%20central%20vision
[3] https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/macular-edema
[4] *Id.*
[5] *Id.*

macula.[6] In Wet AMD, abnormal blood vessels grow develop under the macula and break, bleed, and leak fluid.[7] If left untreated, Wet AMD can result in rapid and severe loss of central vision.[8]

Additionally, blocked blood vessels can cause fluid to leak into the center of the retina.[9] MEfRVO refers to the swelling that results.[10] This condition can also lead to vision loss.[11]

II. BCBS AL's Prior Authorization Policy

On February 2, 2021, BCBS AL updated its prior authorization policy on aflibercept, effective as of July 1, 2021.[12] The policy requires patients to try and fail on one of three bevacizumab medications before the health plan will provide coverage for aflibercept. Yet, while aflibercept is has received FDA approval for Wet AMD, MEfRVO, DME, and DR,[13] bevacizumab has not. Instead, bevacizumab is indicated for metastatic colorectal cancer.[14] In other words, patients must take an off-label medication before they can access the medication that is meant to treat their condition. Moreover, bevacizumab must be compounded in order to be administered for eye disease.[15]

III. Off-Label Use

We recommend against forcing patients to step through off-label bevacizumab medications. The American Society of Retinal Specialists (ASRS) specifically counsels against "step therapy policies that require the off-label use of [bevacizumab]."[16] ASRS emphasizes that "step-therapy requirements interfere with medical decision-making and often delay getting patients the right treatment at the right time. For some patients, this could result in unrecoverable sight loss."[17] Instead, BCBS AL should honor the patient-provider relationship and allow the provider to determine which medication is right for the patient.

IV. Compounding

BCBS AL's policy requiring patients to try and fail on a compounded medication before they can access an FDA-approved medication for Wet AMD, MEfRVO, DME, and DR places patients at risk for unnecessary harm. The FDA has stated that compounded products do not have

---

[6] *Id.*
[7] https://visionaware.org/your-eye-condition/age-related-macular-degeneration-amd/treatments-for-wet-macular-degeneration/#:~:text=In%20wet%20(neovascular%2Fexudative),severe%20loss%20of%20central%20vision.
[8] *Id.*
[9] https://maculardegeneration.net/clinical/macular-edema-following-retinal-vein-occlusion
[10] *Id.*
[11] *Id.*
[12] https://al-policies.exploremyplan.com/portal/web/medical-policies/-/ph-90026?print=1
[13] https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/125387s061lbl.pdf
[14] https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125085s319lbl.pdf; https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761028s004lbl.pdf; https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761099s000lbl.pdf
[15] https://www.biopharmadive.com/news/could-new-fda-compounding-guidelines-stop-avastin-use-in-amd/400089/
[16] https://www.asrs.org/advocacy/step-therapy
[17] *Id.*

the same safety, quality, and efficacy assurances as FDA-approved drugs.[18] For example, in 2019, a Massachusetts federal court sentenced a former supervisory pharmacist of a compounding center to eight years in prison in connection with a nationwide fungal meningitis outbreak that killed 64 and caused infections in 793 patients.[19] The outbreak was caused by poorly compounded products.[20]

Of particular relevance here, the FDA issued an alert warning health care providers of risks associated with compounded bevacizumab in 2011.[21] Repackaged intravitreal injections of bevacizumab resulted in at least 12 patients suffering sight-threatening endophthalmitis infections in the Miami area.[22] The cause of the infections was contaminated injections from improper compounding of bevacizumab.[23] As such, the FDA advised health care professionals to be aware that repackaging sterile drugs without taking aseptic measures may diminish drug sterility and increase patients' risk of infection.[24] FDA inspections continue to result in recalls of bevacizumab.[25]

Likewise, a lawsuit against the U.S. Department of Veterans Affairs alleged that five individuals received bacteria-tainted shots of bevacizumab in a VA hospital in Nashville.[26] The complaint included assertions that the contaminated, compounded drug caused blindness and brain damage in one of the patients who received the injection.[27] Other reports noted that five patients with macular degeneration were blinded at the VA Sepulveda Ambulatory Care Center in California after receiving bevacizumab that was believed to have been compounded at a VA pharmacy.[28] As such, compounding drugs present greater risks than obtaining a prescription drug, such as aflibercept, which must go through strict manufacturing and distributing protocols.

V. Care Delays

As stated above ineffective treatment of Wet AMD, MEfRVO, DME, and DR can result in rapid and severe loss of central vision. As such, requiring patients to step through a medication, especially off-label medication, before accessing a treatment that was prescribed to them and approved by FDA for their condition can result in care delays and disease progression. Forcing patients to step through an off-label medication, which may not provide them with any clinical benefit, could result in the patient missing an important treatment window where the progression of the condition can be slowed. For example, a patient in the UK with Wet AMD who received a

---

[18] https://www.fda.gov/drugs/human-drug-compounding/compounding-and-fda-questions-and-answers#:~:text=Compounded%20drugs%20can%20serve%20an,to%20potentially%20serious%20health%20risks
[19] https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/january-31-2018-new-england-compounding-center-pharmacist-sentenced-role-nationwide-fungal
[20] *Id.*
[21] https://www.healio.com/news/ophthalmology/20120331/fda-issues-alert-after-repackaged-bevacizumab-causes-endophthalmitis-infections-in-florida
[22] *Id.*
[23] *Id.*
[24] *Id.*
[25] https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/pacifico-national-inc-dba-amex-pharmacy-issues-voluntary-nationwide-recall-all-lots-bevacizumab
[26] https://www.reviewofoptometry.com/article/a-tainted-view
[27] *Id.*
[28] *Id.*

delayed referral to an ophthalmologist lost a significant portion of his vision and suffered irreversible damage within the span of a few months while awaiting treatment.[29]

VI. Conclusion

For the reasons stated above, Aimed Alliance requests that BCBS AL withdraw its requirement that patients with Wet AMD, MEfRVO, DME, and DR step through off-label, compounded bevacizumab before being permitted to access aflibercept. If you would like to discuss this matter further, you can contact me at sworthy@aimedalliance.org.

Sincerely,

Stacey Worthy
Counsel

[29] https://www.penningtonslaw.com/case-studies/settlement-for-patient-whose-delay-in-treatment-for-wet-amd-caused-irreversible-loss-of-eyesight