PART B DRUG MEDICAL/PHARMACY	ASPIRE HEALTH	Effective Date: January 1, 2024	
		Policy #: Eylea (aflibercept)	
	EYLEA (AFLIBERCEPT)	**Review Date:** 11/29/2023	**Applicable to:** ☑ Medicare Advantage ☐ Commercial ☐ Elevance Health HMO ☐ Blue Shield Trio
	Approver's Name & Title QI & UM Drug Subcommittee		

Aspire Health Plan applies medical drug clinical criteria as a reference for medical policy information only. Federal and state laws or requirements, contract language, and Plan benefit may take precedence over the application of these clinical criteria. Please consult the applicable certificate or contract for benefit details. This policy is subject to revision at the discretion of the Plan and is therefore subject to change. Refer to the disclaimer section below for more information.

POLICY

This policy addresses the coverage of Eylea (aflibercept) for ophthalmic use.

APPLICABLE HCPCS

J0178: Injection, aflibercept, 1 mg; 1 billable unit = 1 mg

EYLEA HD temporary miscellaneous HCPCS code:
J3490: Unclassified drugs
J3590: Unclassified biologicals
C9399: Unclassified drug or biologic (limited to HOPD and ASC claims for Medicare beneficiaries)

Available as:
- 2mg/0.05mL single-dose vial (Eylea)
- 2mg/0.05mL single-dose prefilled syringe (Eylea)
- 8mg/0.07mL (114.3mg/mL single-dose vial) (Eylea HD)

CLINICAL CRITERIA

A. INITIAL THERAPY

Eylea (aflibercept) may be authorized when **ALL** of the following are present:

1. Clinical diagnosis of **ONE or more** of the following:
   a. Neovascular (wet, or exudative) age-related macular degeneration (AMD)
   b. Diabetic macular edema
   c. Diabetic retinopathy (in patients with diabetic macular edema)
   d. Macular edema following central or branch retinal vein occlusion

AND

2. No active intraocular inflammation; **AND**

3. No concurrent ocular or periocular infection; **AND**

4. Eylea (aflibercept) is being prescribed as monotherapy: Member is not on additional ophthalmic vascular endothelial growth factor (VEGF) inhibitors (i.e., aflibercept, ranibizumab, pegaptanib, bevacizumab); **AND**

5. Baseline best corrected visual acuity (BCVA) is assessed prior to treatment and will be assessed periodically during treatment.

B. REAUTHORIZATION / CONTINUATION OF THERAPY CRITERIA

Eylea (aflibercept) may be authorized for continuation of therapy when ALL the following are met:

1. Member continues to meet the initial therapy criteria (as stated above); **AND**

2. Absence of adverse events from intravitreal injections of Eylea (e.g., endophthalmitis and retinal detachments, increase in intraocular pressure, arterial thromboembolic events); **AND**

3. Positive response to therapy (e.g., improvement or maintenance in BCVA or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss) and continued administration is necessary for the maintenance treatment of the condition; **AND**

4. Documentation of administration records showing dates and eye(s) administered, along with documentation of member compliance with treatment plan.

STEP THERAPY

Step therapy criteria do not apply for members who are currently being treated with the requested medications. Step therapy is only applied for members that are new to therapy (have not received the requested drug in the last 365 days.

EXCEPTION: Members meeting the clinical criteria with the following conditions are not required to meet the Step Therapy requirements:

1) Diagnosis of Diabetic Macular Edema and baseline visual acuity in the affected eye(s) is less than or equal to 20/50, OR
2) Retinal / vitreous hemorrhage.

A. PREFERRED PRODUCT(S): AVASTIN (no step therapy required)

B. NONPREFERRED PRODUCT, Eylea (aflibercept), may be authorized when all of the clinical criteria above are met **AND** the member meets the following criteria for a non-preferred intravitreal VEGF inhibitors:

1. Inadequate response to a trial of the *preferred agent, bevacizumab (Avastin); **or**

2. History of contraindication or adverse event(s) to Avastin (bevacizumab); **or**

3. Member has been on the requested agent within the past 365 days.

DOSAGE AND AUTHORIZATION TIMEFRAMES

1. Recommended / Maximum Dose

Indication	Initial / Maintenance Dosing	Maximum Dosing
Neovascular (wet, or exudative) age-related macular degeneration **(Eylea, Eylea HD)**	*Eylea* Initial: 2 mg every 4 weeks for the first 3 months of treatment Maintenance: Every 4 to 8 weeks until a dosing frequency of every 12 weeks. *Eylea HD* Initial: 8 mg every 4 weeks for the first 3 months Maintenance: 8 mg every 8 to 16 weeks.	*Eylea* 2 mg per eye; 1 vial per eye every 28 days (2 units per eye every 28 days)
Diabetic Macular Edema (DME) & Diabetic Retinopathy (DR) in patients with DME **(Eylea, Eylea HD)**	*Eylea* Initial: 2 mg every 4 weeks for the first 5 months of treatment Maintenance: Every 4 to 8 weeks *Eylea HD* Initial: 8 mg every 4 weeks for the first 3 months Maintenance: DME: 8 mg every 8 to 16 weeks. DR: 8 mg every 8 to 12 weeks	*Eylea* 2 mg per eye; 1 vial per eye every 28 days (2 units per eye every 28 days)
Macular edema following central or branch retinal vein occlusion **(Eylea only)**	*Eylea* 2 mg by every 4 weeks.	2 mg per eye; 1 vial per eye every 28 days (2 units per eye every 28 days)
Retinopathy of Prematurity (ROP) **(Eylea only)**	*Eylea* 0.4 mg per eye(s); may repeat dose(s) after a minimum interval of 10 days	0.4 mg per eye(s); may repeat dose(s) after a minimum interval of 10 days

2. Authorization Period:

   a. May be authorized for 12 months and reauthorized with continuation of therapy criteria.

   b. Frequency is regarded as excessive when services are performed more frequently than indicated on the FDA-approved labeling or generally accepted by guidelines or consensus, and a rationale for the additional services is not documented. Dosage and frequency should be in accordance with the FDA label or CMS-recognized compendia (for off-label use). Services rendered in excess of the established standard of care may be subjected to review.

3. Limitations

   a. It is not reasonable and necessary to inject more than one anti-VEGF medication (e.g., aflibercept, pegaptanib, brolucizumab, bevacizumab, ranibizumab, faricimab-svoa, etc.) in the same eye during the same treatment session. It is not typical to inject one anti-VEGF medication in one eye and another in the other eye. If different medications are injected into each eye during the same date of service, the rationale for this therapy must be documented in the medical record and the billing modifier [right (RT) and left (LT) modifiers] must be appended to the correct drug. Intravitreal injection for the treatment of macular edema more frequently than every 4 weeks regardless of which drug is used for any given injection i.e. alternating drugs every 2 weeks will not be covered.

   b. Concurrent use of more than one VEGF inhibitor in the same eye: The safety and effectiveness of combination use of VEGF inhibitors for ocular indications has not been established and is currently not the standard of care according to clinical evidence and guidelines.

DRUG INFORMATION

PHARMACOLOGIC CATEGORY: Ophthalmic Agent; Vascular Endothelial Growth Factor (VEGF) Inhibitor

ROUTE OF ADMINISTRATION: Intravitreal Injection

PRODUCTS

1. Eylea (aflibercept) 2 mg is indicated for the treatment of patients with neovascular (Wet) age-related macular degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR) in patients with DME, and retinopathy of prematurity (ROP).

2. Eylea HD (aflibercept) 8 mg is indicated for the treatment of patients with neovascular (Wet) AMD, DME, and DR in patients with DME.

FDA-APPROVED INDICATIONS

1. Neovascular (wet, or exudative) AMD: Aflibercept is administered by intravitreal injection every 4 weeks for the first 3 months of treatment, then continued by intravitreal injection every 4 to 8 weeks. After 1 year of therapy, the dosing frequency may be extended by 2 weeks in eyes with inactive disease until a dosing frequency of every 12 weeks is reached, assuming the disease remains inactive.

2. DME: Aflibercept is administered by intravitreal injection every 4 weeks for the first 5 injections, and then continued by intravitreal injection every 4 to 8 weeks.

3. DR: Aflibercept is administered by intravitreal injection every 4 weeks for the first 5 injections, and then continued by intravitreal injection every 4 to 8 weeks.

4. Macular edema following central or branch retinal vein occlusion: Aflibercept is administered by intravitreal injection every 4 weeks.

5. ROP: 0.4 mg as a single intravitreal injection in the affected eye(s); may repeat dose(s) after a minimum interval of 10 days.

COMPENDIAL APPROVED (OFF-LABELED) USES: NONE

CONTRAINDICATIONS:
Known hypersensitivity to aflibercept or any component of the formulation; current ocular or periocular infection; active intraocular inflammation.

OTHER CONSIDERATIONS:

Monitoring Parameters

Post-injection complications, including increased intraocular pressure, endophthalmitis, and retinal detachment.

CLINICAL SUMMARY / APPENDIX

Eylea (aflibercept) is indicated for the treatment of patients with wet AMD, DME, DR, macular edema following retinal vein occlusion, and ROP (FDA approval: November 18, 2011).

Eylea HD is an ophthalmic VEGF inhibitor that was FDA-approved on August 18, 2023, for the treatment of neovascular (wet) age-related macular degeneration, DME, and DR. It is a high-dose (HD) version of Eylea (aflibercept 2 mg) that offers the possibility of extended-interval dosing with similar results compared to its predecessor, Eylea. Administration of Eylea HD allows for extended-dose intervals of up to 16 weeks for DME and wet AMD, and 12 weeks in DR. Eylea is usually administered every 4 weeks, which may be extended to once every 8 weeks (2 months), depending on the condition.

The FDA approval of the higher dose is based on the 48-week results of PULSAR and PHOTON pivotal trials evaluating Eylea HD compared with Eylea 2 mg. Both trials met their primary endpoint, with Eylea HD demonstrating non-inferior and clinically equivalent vision gains at 48 weeks with both 12- and 16-week dosing regimens after three initial monthly doses.

The most common adverse reactions of Eylea HD were cataract, conjunctival hemorrhage, intraocular pressure increased, ocular discomfort/eye pain/eye irritation, vision blurred, vitreous floaters, vitreous detachment, corneal epithelium defect, and retinal hemorrhage.

REFERENCES

Government Agency

Centers for Medicare and Medicaid Services (CMS). Medicare coverage database (no National Coverage Determination identified; no applicable LCD identified). Available from CMS.

Prescribing Information

1. Eylea (aflibercept) [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals Inc; March 2023.
2. Eylea HD (aflibercept) [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals Inc; August 2023.

Peer-reviewed Literature, Guidelines, and Consensus

1. Anguita R, Tasiopoulou A, Shahid S, Roth J, Sim SY, Patel PJ. A review of aflibercept treatment for macular disease. Ophthalmology and Therapy 2021;10(3):413-428. DOI: 10.1007/s40123-021-00354-1.
2. Milliman Care Guidelines (MCG). Ambulatory Care 27th Edition. ACG: A-0680 (AC). 2023.
3. Scott IU, et al. Effect of bevacizumab vs aflibercept on visual acuity among patients with macular edema due to central retinal vein occlusion: the SCORE2 randomized clinical trial. Journal of the American Medical Association 2017;317(20):2072-2087. DOI: 10.1001/jama.2017.4568.
4. Sivaprasad S, et al. Clinical efficacy of intravitreal aflibercept versus panretinal photocoagulation for best corrected visual acuity in patients with proliferative diabetic retinopathy at 52 weeks (CLARITY): a multicentre, single-blinded, randomised, controlled, phase 2b, non-inferiority trial. Lancet 2017;389(10085):2193-203. DOI: 10.1016/S0140-6736(17)31193-5.
5. Sun JK, Jampol LM. The Diabetic Retinopathy Clinical Research Network (DRCR.net) and its contributions to the treatment of diabetic Retinopathy. Ophthalmic Research 2019;62(4):225-230. DOI: 10.1159/000502779.
6. Yeh S, et al. Therapies for macular edema associated with central retinal vein occlusion: A report by the American Academy of Ophthalmology. Ophthalmology 2015;122(4):769-778. DOI: 10.1016/j.ophtha.2014.10.013. (Reaffirmed 2022 Jul).

IMPORTANT REMINDER

This Medicare Part B Step Therapy Medical Necessity Guideline is provided for informational purposes only and neither constitutes nor replaces professional medical advice. Physicians, hospitals, and other providers are expected to administer or use drugs/biologicals in the most effective and clinically appropriate manner. Treating physicians and other health care providers are solely responsible for all medical care decisions. In accordance with the member's Evidence of Coverage (EOC), every benefit plan has its own coverage provisions, limitations, and exclusions. In the event of a conflict between this policy and the member's EOC, the member's EOC provisions will take precedence.

Aspire Health Plan (AHP) adheres to Medicare guidelines, including National Coverage Determination (NCD), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and other relevant Medicare manuals established by CMS. Compliance with these guidelines is required when applicable. Refer to the CMS website at http://www.cms.hhs.gov. For the most up-to-date Medicare policies and coverage, please search the Medicare Coverage Database. All LCDS are the same for each state within a Jurisdiction. Medicare Part B Administrative Contractor (MAC) for CA [Jurisdiction E (1)]: Active LCDs - JE Part B – Noridian (noridianmedicare.com). In the event of a discrepancy between this policy and the Medicare NCD or LCD, the Medicare NCD/LCD will govern.

This policy is utilized by AHP to determine coverage in the absence of applicable CMS Medicare guidelines. Please refer to the links provided in the References section to access the Medicare source materials that were used for developing this resource document. This document does not serve as a substitute for the official Medicare source materials that provide detailed information on Medicare coverage requirements. In the event of a conflict between this document and Medicare source materials, the Medicare source materials will take precedence.

The inclusion of a code in this policy does not imply that the health service it describes is covered or not covered. Benefit coverage for health services is determined by the member-specific plan document and applicable laws that may mandate coverage for a particular service. Inclusion of a code does not imply or guarantee reimbursement or payment of a claim. Other Policies and Standards may also apply. Providers are expected to retain or have access to the necessary documentation when requested in order to support coverage.

POLICY HISTORY

Version	Date	Revision Author/Title	Summary of Changes
1	11/29/2023		New Policy.