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Policy Number: C5674-A

Eylea (aflibercept) and Biosimilars

PRODUCTS AFFECTED

Eylea (aflibercept), Eylea HD (aflibercept), Pavblu (aflibercept-ayyh)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Neovascular (Wet) Age-Related Macular Degeneration (AMD), Macular Edema Following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR), Retinopathy of prematurity (ROP)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

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A. ALL INDICATIONS:

1. Documented diagnosis of ANY of the following: Neovascular (Wet) age-related macular degeneration, Macular edema following retinal vein occlusion (Eylea/Pavblu only), Diabetic macular edema, Diabetic retinopathy, Retinopathy of prematurity (Eylea only)
   AND
2. Documentation of baseline visual status with notation of eye(s) being treated [DOCUMENTATION REQUIRED]
   AND
3. Documentation of an inadequate response (defined as 1-2 injections with minimal to no improvement), serious side effects, or contraindication to bevacizumab OR bevacizumab is indicated by the provider as unavailable and there is documentation of an inadequate response, serious side effects or contraindication to ranibizumab
   EXCEPTION: Members with diagnosis of Diabetic Macular Edema and baseline visual acuity of 20/50 or worse do NOT have to meet this criterion
   AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to aflibercept include: ocular or periocular infections, active intraocular inflammation, known hypersensitivity to aflibercept or any of the excipients in the requested product]
   AND
5. (a) IF THIS IS A PHARMACY BENEFIT REQUEST FOR A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or serious side effects to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. Documentation of medication(s) tried, dates of trial(s) and reason for treatment failure(s) is required.
   AND
   (b) If request is for reference product with a biosimilar available for initial or continuation of therapy requests: Documentation of a trial and failure, serious side effects or contraindication to a majority (not more than 3) biosimilar product(s) is required (unless otherwise specified per applicable state regulations and/or there is data demonstrating clinical superiority of reference drugs over the FDA approved biosimilar drugs).
   [DOCUMENTATION REQUIRED: Document when the preferred biologic product or biosimilar was tried and the length of the trial period. Provide specific clinical documentation of therapeutic failure on the preferred biologic product or biosimilar whenever possible. Describe the medical problem caused by the preferred referenced biologic. Vague and non-descriptive symptoms are not adequate rationale (e.g., stomachache).]
   MOLINA REVIEWER NOTE: For Illinois Marketplace, please see Appendix.
   OR
6. FOR INITIAL OR CONTINUATION OF THERAPY REQUESTS OF A PHYSICIAN ADMINISTERED MEDICATION: BIOSIMILAR DRUGS are preferred when requested as a physician administered drug per applicable state regulations and/or there is a lack of data demonstrating clinical superiority of reference drugs over the FDA approved biosimilar drugs. A reference medication is approved under the following conditions:
   a. Treatment with at least two associated biosimilar drug(s) has been ineffective, resulted in serious side effects, or is contraindicated (i.e., an allergic reaction to a specific inactive ingredient in the preferred biologic product or biosimilar OR an adverse reaction to a specific inactive ingredient in the preferred biologic product or biosimilar OR therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure while taking the preferred biologic product or biosimilar documented by patient diary or medical charted notes)

   [DOCUMENTATION REQUIRED: Document when the preferred biologic product or biosimilar

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was tried and the length of the trial period. Provide specific clinical documentation of therapeutic failure on the preferred biologic product or biosimilar whenever possible. Describe the medical problem caused by the preferred referenced biologic. Vague and non-descriptive symptoms are not adequate rationale (e.g., stomachache).]

CONTINUATION OF THERAPY:

A. ALL INDICATIONS:

1. Reauthorization request is for the same eye(s) as initial authorization
   NOTE: The continuation of therapy criteria is only for the same previously treated eye(s). If member has developed condition in an untreated eye, Prescriber must submit new request with Initial Coverage criteria.
   AND
2. Documentation of improvement or stabilization of disease state (e.g., reduction in rate of progression and frequency of retinopathy, hemorrhage, macular edema, etc.) and visual status [DOCUMENTATION REQUIRED]
   AND
3. Documentation of administration records showing dates and eye(s) administered, along with documentation of member compliance with treatment plan
   AND
4. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified ophthalmologist, ophthalmic surgeon or retinal specialist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

Retinopathy of Prematurity: No restriction
All other indications: 18 years of age and older

QUANTITY:

EYLEA, PAVBLU:

Neovascular (Wet) Age-Related Macular Degeneration (AMD):
Initiation: 2 mg (0.05 mL) intravitreally once every 4 weeks (monthly) per affected eye(s) for the first 3 months
Maintenance: 2 mg (0.05 mL) once every 8 weeks (2 months); however, aflibercept may be dosed as frequently as 2 mg every 4 weeks (monthly)

Macular Edema following Retinal Vein Occlusion (RVO):
2 mg (0.05 mL) intravitreally once every 4 weeks (monthly) per affected eye(s)

Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR):
Initiation: 2 mg (0.05 mL) intravitreally once every 4 weeks (monthly) per affected eye(s) for the first 5 injections
Maintenance: 2 mg (0.05 mL) once every 8 weeks (2 months); however, aflibercept may be dosed as frequently as 2 mg every 4 weeks (monthly)

Maximum Quantity Limits – 2 mg (0.05 mL) intravitreally once every 4 weeks (monthly) per eye

EYLEA:

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Retinopathy of Prematurity (ROP):
0.4 mg (0.01 mL) intravitreally for up to 3 doses per affected eye(s). Treatment interval between doses in the same eye should be at least 10 days.

EYLEA HD:
Neovascular (Wet) Age-Related Macular Degeneration (AMD) and Diabetic Macular Edema (DME):
Initiation: 8 mg (0.07 mL) intravitreally once every 4 weeks for the first three doses
Maintenance: 8 mg (0.07 mL) once every 8 to 16 weeks

Diabetic Retinopathy (DR):
Initiation: 8 mg (0.07 mL) intravitreally once every 4 weeks for the first three doses
Maintenance: 8 mg (0.07 mL) once every 8 to 12 weeks

PLACE OF ADMINISTRATION:
The recommendation is that intravitreal medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility- based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravitreal

DRUG CLASS:
Vascular Endothelial Growth Factor (VEGF) Antagonist

FDA-APPROVED USES:
Eylea (aflibercept) 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), Diabetic Retinopathy (DR), and Retinopathy of Prematurity (ROP)

Eylea HD (aflibercept) is indicated for the treatment of patients with Neovascular (Wet) Age-Related Macular Degeneration (nAMD), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR)

Pavblu (aflibercept-ayyh) 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).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Reserved for State specific information. Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.

State Specific Information
State Marketplace
Illinois (Source: Illinois General Assembly)
"(215 ILCS 134/45.1) Sec. 45.1. Medical exceptions procedures required. (c) An off-formulary exception request shall not be denied if: (1) the formulary prescription drug is contraindicated; (2) the patient has tried the formulary prescription drug while under the patient's current or previous health insurance or health benefit plan and the

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prescribing provider submits evidence of failure or intolerance; or (3) the patient is stable on a prescription drug selected by his or her health care provider for the medical condition under consideration while on a current or previous health insurance or health benefit plan. (d) Upon the granting of an exception request, the insurer, health plan, utilization review organization, or other entity shall authorize the coverage for the drug prescribed by the enrollee's treating health care provider, to the extent the prescribed drug is a covered drug under the policy or contract up to the quantity covered. (e) Any approval of a medical exception request made pursuant to this Section shall be honored for 12 months following the date of the approval or until renewal of the plan."

Appendix 1:

A biosimilar is a highly similar version of a brand name biological drug that meets strict controls for structural, pharmaceutical, and clinical consistency. A biosimilar manufacturer must demonstrate that there are no meaningful clinical differences (i.e., safety and efficacy) between the biosimilar and the reference product. Clinical performance is demonstrated through human pharmacokinetic (exposure) and pharmacodynamic (response) studies, an assessment of clinical immunogenicity, and, if needed, additional clinical studies.[1]

As costs for biological specialty drugs continue to rise, the growing biosimilar market will benefit providers and patients by broadening biological treatment options and expanding access to these medications at lower costs. Molina Healthcare, Inc. continues to be committed to continually reevaluating preferred strategies and applying innovative cost-controls to ensure patients receive safe, effective, and quality healthcare. This commitment includes potentially creating a preference for biosimilars when value can be added without compromising patient satisfaction and safety.

1. Food and Drug Administration. Biosimilar and Interchangeable Products. Retrieved from https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products. Accessed October 8, 2019.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Clinical trials of aflibercept and other intravitreal VEGF inhibitors in the treatment of wet AMD have shown evidence of efficacy for maintaining or improving visual acuity; however, there is insufficient evidence to determine the superiority of one VEGF agent over the other. The evidence to support the use of one anti-VEGF therapy over another is scant as most of the clinical trials provided data demonstrating comparability, rather than superiority, in safety and efficacy.

Several randomized control trials (RCTs) have been conducted to compare the effects of the frequently used anti-VEGF agents, ranibizumab and bevacizumab (Avastin), for the treatment of wet AMD since bevacizumab has not been FDA approved for intraocular injection and has been more cost-effective than ranibizumab. In addition, two RCTs available found that Avastin, Eylea, and Lucentis were all non-inferior to each other, and therefore, choice of treatment should be based on patient characteristics, side effect profiles, cost, and availability. However, a comparative effectiveness study demonstrated that aflibercept (Eylea) was on average, was more effective at improving vision in patients with a visual acuity of less than or equal to 20/50 (Wells et al. 2015); therefore, in such cases, bevacizumab (Avastin) is not recommended prior to Eylea.

The Diabetic Retinopathy Clinical Research Network (DRCR.net) conducted a comparative effectiveness trial comparing the three commonly used anti-VEGF agents [aflibercept (Eylea), bevacizumab (Avastin), and ranibizumab (Lucentis)] for center-involved DME associated with visual impairment (Well et al. 2015). All three agents were noted to improve vision, on average, with treatment group differences varying according to initial visual acuity in the previously reported 1-year results. No apparent differences in visual acuity, on average, were identified among the groups when baseline visual acuity impairment was mild (20/32 to 20/40); however, at lower levels of visual acuity (20/50 to 20/320), aflibercept was more effective at improving vision than the other two agents. No statistically significant differences in pre-specified ocular or systemic safety events among the 3 anti-VEGF agents were identified.

The comparative effectiveness study for center-involved DME demonstrated vision gains in all three drugs

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at the 2-year visit, with an average of almost half the number of injections, slightly decreased frequency of visits, and decreased amounts of focal/grid laser treatment in all 3 groups in the second year. Wells et al. (2016) concluded in a 2-year randomized trial for center-involved DME that all 3 anti-VEGF groups had vision improvements at 2 years with fewer injections. At 2 years, in eyes with better baseline visual acuity, there still were no meaningful differences identified in mean visual acuity change among the treatment groups. Visual acuity outcomes were similar among treatment groups for eyes with baseline VA 20/32 - 20/40. In eyes with baseline VA of 20/50 or worse (20/50 - 20/320), the advantage of aflibercept (Eylea) over ranibizumab (Lucentis), noted at 1 year, had decreased and was no longer statistically significant at 2 years. Aflibercept (Eylea) remained superior to bevacizumab (Avastin). Overall, few eyes in any group lost substantial amounts of vision, regardless of the baseline visual acuity. More APTC events with ranibizumab. Rates of ocular adverse events, including endophthalmitis and post-injection inflammation, remained low through 2 years with all 3 agents; however, systemic Anti-Platelet Trialists' Collaboration (APTC) events were higher in the ranibizumab group over two years justifies continued evaluation in future studies.

A systematic review evaluated the effectiveness and safety of intravitreal injections of aflibercept versus ranibizumab, bevacizumab, or sham for treatment of patients with neovascular AMD from two RCTs (total of 2457 participants, 2457 eyes) with neovascular AMD (Sarwar S, et al.; Cochrane Review 2016). The meta-analysis evaluated VIEW 1 and VIEW 2 trials (N=2457 participants, 2457 eyes) comparing aflibercept with ranibizumab in patients with subfoveal neovascular AMD who were treatment naive in the study eye. Both studies randomized patients to treatment with intravitreal injections of aflibercept 0.5 mg every 4 weeks, aflibercept 2 mg every 4 weeks, aflibercept 2 mg every 8 weeks after 3 initial monthly injections, or ranibizumab 0.5 mg every 4 weeks for a primary treatment period of 52 weeks. During a follow-up phase from weeks 52 to 96, all regimens were switched from the fixed monthly or bimonthly regimen to an as-needed regimen with a minimum quarterly dose. Changes in visual acuity, both gains and losses, were similar among aflibercept- and ranibizumab-treated eyes. Overall improvement in visual acuity correlated with anatomic improvements (e.g., retinal thickening, choroidal neovascularization [CNV] size) for both agents. At one year, participants in the aflibercept groups showed mean change in best- corrected visual acuity (BCVA) from baseline similar to that of participants in the ranibizumab groups. At two years, the mean change in BCVA from baseline was 7.2 ETDRS letters for aflibercept groups versus
7.9 for ranibizumab groups. At one year, the proportion of eyes that achieved dry retina was similar between aflibercept and ranibizumab groups. The authors concluded that current available information on adverse effects of each medication suggests that the safety profile of aflibercept is comparable with that of ranibizumab. Overall, occurrence of serious systemic adverse events was similar and comparable in aflibercept- and ranibizumab-treated groups at one year. The eight-week dosing regimen of aflibercept represents reduced treatment requirements in comparison with monthly dosing regimens and thus has the potential to reduce treatment burden and risks associated with frequent injections. Sarwar et al. noted that no clinical trial that compared aflibercept versus bevacizumab for the treatment of individuals with neovascular AMD; however, several studies have compared ranibizumab versus bevacizumab for outcomes of neovascular AMD (Solomon 2016).

Several RCTs have compared the effects of the frequently used anti-VEGF agents, ranibizumab (Lucentis) and bevacizumab (Avastin), for the treatment of wet AMD since bevacizumab has not been FDA approved for intraocular injection and has been more cost-effective than ranibizumab.

Solomon et al. conducted a systematic review of the most frequently used intravitreal anti-VEGF agents to treat neovascular (wet) AMD, bevacizumab and ranibizumab. The review included only RCTs in which the 2 anti-VEGF agents had been compared directly. The authors located 6 RCTs (with 2806 participants) and compared the effect of intravitreal injections of bevacizumab relative to ranibizumab with respect to several different outcomes that are important to patients with wet AMD and their ophthalmologists. The study found no important difference between the 2 anti-VEFG agents for clinical outcomes such as BCVA, visual function, and lesion morphology through 2 years of follow-up. There is also no important difference in the most serious ocular complications; however, rates of serious ocular adverse events were small, that is, no more than 1%.

Overall efficacy results, in terms of visual acuity, appear similar for the drugs that have been compared. For example, efficacy between bevacizumab and ranibizumab was comparable in the Comparison of AMD

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Treatment Trials (CATT) and the Inhibition of VEGF in Age-related Choroidal Neovascularization trial (IVAN study). Aflibercept and ranibizumab were comparable for maintaining vision (loss of <15 letters) in the VIEW 1 and VIEW 2 trials. Most recently, brolucizumab was noninferior to aflibercept in the HAWK and HARRIER trials. Head-to-head trials have not compared bevacizumab versus aflibercept, or brolucizumab versus bevacizumab or ranibizumab. There may be differences among anti-VEGF agents in terms of resolution of fluid on OCT and durability of anti-VEGF effect in an individual patient. While it is not clear what produces individual variations in response to anti-VEGF agents, hypotheses such as anti- VEGF resistance and tachyphylaxis have been explored.

Bevacizumab and ranibizumab had equivalent effects on visual acuity when administered on the same dosing regimen.

· CATT was a multicenter clinical trial that compared the safety and effectiveness of bevacizumab to ranibizumab and an individualized dosing regimen (as needed, or PRN) to monthly injections. The primary outcome was the mean change in visual acuity at 1 year, with a non-inferiority limit of 5 letters on the eye chart. Bevacizumab administered monthly was equivalent to ranibizumab administered monthly. Bevacizumab administered as needed was equivalent to ranibizumab as needed. Ranibizumab PRN was equivalent to monthly ranibizumab, although the comparison between bevacizumab as needed and monthly bevacizumab was inconclusive. Further follow-up at two years showed that the two drugs remained comparable in both efficacy and safety, but the PRN arms together did not perform as well in terms of maintaining the visual gains at the end of year one compared with the two monthly injection arms, especially in the bevacizumab PRN group. At one year, bevacizumab and ranibizumab had equivalent effects on visual acuity when administered according to the same schedule. Ranibizumab given as needed with monthly evaluation had effects on vision that were equivalent to those of ranibizumab administered monthly.

· IVAN study (2012, 2013) enrolled 610 patients and found that for the primary outcome of best visual acuity at two years, bevacizumab was neither non-inferior nor inferior to ranibizumab. There was no difference in mortality, atherothrombotic events, or hospital admission between the two drugs. A meta-analysis combining results from one-year data of the CATT trial and two-year data from the IVAN trial found that bevacizumab was non-inferior to ranibizumab for visual acuity; additional randomized trials comparing the two drugs at two years also demonstrated non-inferiority for bevacizumab (Kodjikian L, et al. 2013) or equivalent efficacy (Berg K, et al. 2016)

American Academy of Ophthalmology (AAO)
Age-Related Macular Degeneration Preferred Practice Patterns (PPO) (2019)

The AAO (2019) noted that treatments for neovascular AMD include intravitreal injection of anti-VEGF agents, photodynamic therapy, and use of antioxidant vitamins and zinc supplementation for slowing disease progression. Anti-VEGF agents (aflibercept, bevacizumab [off-label use], pegaptanib, and ranibizumab) are considered first-line treatment and most effective way to manage neovascular AMD. The guidelines did not recommend Macugen (pegaptanib) stating that unlike the other anti-VEGF agents that are currently available (ranibizumab, aflibercept, and bevacizumab), pegaptanib treatment does not improve visual acuity on average in patients with new-onset neovascular AMD and is rarely used in current clinical practice.

Diabetic Retinopathy PPP (2019) According to the guidelines, treatment with laser, anti-VEGF agents, or intravitreal corticosteroids is cost- effective for managing DR to varying degrees. Intravitreal anti-VEGF agents are effective in the treatment of center-involved DME with vision loss. Laser photocoagulation surgery remains the preferred treatment for non-center-involved DME and pan-retinal photocoagulation surgery remains the mainstay treatment for proliferative. The PPP notes that the most serious complication of anti-VEGF injections is infectious endophthalmitis with rates between 0.019% and 0.09% in clinical trial settings and other complications, such as retinal detachment, cataract formation, and sustained elevated IOP are rare.
Retinal Vein Occlusions PPP (2019)

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The AAO (2019) notes that macular edema may complicate both CRVOs and BRVOs and the first-line of treatment for associated macular edema is anti-VEGFs. Intravitreal corticosteroids, with the associated risk of glaucoma and cataract formation, have demonstrated efficacy. Also, laser photocoagulation surgery in BRVO has a potential role in treatment.

Efficacy and safety of aflibercept in retinopathy of prematurity (ROP) was derived from BUTTERFLEYE and FIREFLEYE. BUTTERFLEYE was a 52-week study. FIREFLEYE included 24 weeks of treatment and follow-up. FIREFLEYE NEXT was an observational follow-up of FIREFLEYE through week 52. Both studies assessed the efficacy, safety and tolerability of Eylea in randomized, 2 arm, open label, parallel group studies. The studies were conducted in pre-term infants with ROP providing a comparison between EYLEA treatment and laser photocoagulation therapy (laser). Re-treatment with aflibercept, if required, was administered up to 2 times in a particular eye, with at least 28 days between consecutive injections. Eligible patients had a maximum gestational age at birth of 32 weeks or a maximum birth weight of 1500 g, had to weigh > 800 g on the day of treatment and had treatment-naïve ROP classified according to the International Classification for Retinopathy of Prematurity (IC-ROP 2005) in at least one eye. The primary efficacy endpoint of each study was the proportion of patients with absence of active ROP and unfavorable structural outcomes (retinal detachment, macular dragging, macular fold, retrolental opacity) at week 52 of chronological age. The proportion of patients without clinically significant reactivations of ROP who also did not develop unfavorable structural outcomes was higher in each arm of each study than would have been expected in infants who had not received treatment. Neither trial demonstrated superiority of one arm compared to the other arm. Neither trial demonstrated inferiority of one arm compared to the other arm. Anti-VEGF therapy is effective for treating ROP and bevacizumab, ranibizumab, and aflibercept have been used. There are no prospective comparison studies.

Eylea HD (aflibercept) is a high dose formulation of Eylea. The approval of Eylea HD was based on the 48-week results of the Phase 3, double-masked, active-controlled PULSAR and PHOTON trials, which compared Eylea HD to Eylea 2 mg in wAMD and DME, respectively. Both trials met their primary endpoint, with Eylea HD demonstrating noninferiority in best corrected visual acuity (BCVA) with both 12- and 16-week dosing regimens in wAMD and DME, compared with Eylea, given as an 8-week dosing regimen after initial monthly doses.
The DR indication for Eylea HD was based on data derived from the PHOTON study, which evaluated the proportion of patients with a ≥2-step improvement in the change in the Early Treatment Diabetic Retinopathy Study–Diabetic Retinopathy Severity Scale (ETDRS–DRSS) to determine noninferiority to Eylea. For this measure, the group that received Eylea HD every 12 weeks met the noninferiority criteria; however, the group that received Eylea HD every 16 weeks did not.

Biosimilarity of Pavblu has been demonstrated for the condition(s) of use (e.g., indication(s), dosing regimen(s), strength(s), dosage form(s), and route(s) of administration) described in the prescribing information.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of aflibercept are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to aflibercept include: Ocular or periocular infections, active intraocular inflammation, hypersensitivity to aflibercept or any of the excipients in the requested product.

Exclusions/Discontinuation:
Do not use with other ophthalmic VEGF inhibitors (i.e., bevacizumab, brolucizumab, faricimab, ranibizumab, etc.).

OTHER SPECIAL CONSIDERATIONS:
None

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HCPCS CODE	DESCRIPTION
J0178	Injection, aflibercept, 1 mg
J0177	Injection, aflibercept HD, 1 mg
Q5147	Injection, aflibercept-ayyh (pavblu), biosimilar, Pavblu

AVAILABLE DOSAGE FORMS:
Eylea SOLN 2MG/0.05 ML single-dose vial kit
Eylea SOSY 2MG/0.05ML prefilled syringe
Eylea HD SOLN 8MG/0.07ML single-dose vial
Pavblu SOLN 2MG/0.05ML single-dose vial
Pavblu SOSY 2MG/0.05ML single-dose prefilled syringe

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Appendix Contraindications/Exclusions/Discontinuation Coding/Billing Information References	Q4 2025
REVISION- Notable revisions: Criteria Name Products Affected Required Medical Information FDA-Approved Uses Appendix Background Available Dosage Forms References	Q1 2025
REVISION- Notable revisions: Coding/Billing Information Template Update Coding/Billing Update References	Q4 2024

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REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Quantity Drug Class FDA-Approved Uses Background Contraindications/Exclusions/Discontinuation Coding/Billing Information Available Dosage Forms References	Q4 2023
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Age Restrictions Quantity FDA-Approved Uses Background References	Q2 2023
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Duration of Approval Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file

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