Drug Coverage Policy

Effective Date……02/01/2026
Coverage Policy Number……IP0540
Policy Title……Aflibercept Products

Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Aflibercept Products

- Eylea® (aflibercept intravitreal injection – Regeneron)
- Eylea® HD (aflibercept intravitreal injection – Regeneron)
- Pavblu™ (aflibercept-ayyh intravitreal injection – Amgen)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used

as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview
Aflibercept is a vascular endothelial growth factor (VEGF) inhibitor.[1-3] Ophthalmic aflibercept products (Eylea, Pavblu, and Eylea HD) are given intravitreally for the treatment of ophthalmic conditions. Pavblu is a biosimilar to Eylea, indicating no clinically meaningful differences in safety and effectiveness and the same mechanism of action, route of administration, and dosage form as Eylea.[1,2] However, minor differences in clinically inactive components are allowed.

Intravitreal aflibercept injection (Eylea and Pavblu) is indicated for the following uses:[1,2]
- **Diabetic macular edema**.
- **Diabetic retinopathy**.
- **Macular edema following retinal vein occlusion**.
- **Neovascular (wet) age-related macular degeneration**.
- **Retinopathy of prematurity**

Eylea HD, a high dose aflibercept product, is indicated for the following uses:[3]
- **Diabetic macular edema**.
- **Diabetic retinopathy**.
- **Macular edema following retinal vein occlusion.**
- **Neovascular (wet) age-related macular degeneration**.

Dosing Information:
The recommended dosing for Eylea and Pavblu for each indication is as follows:[1,2]
- Diabetic macular edema: 2 mg via intravitreal injection once every 4 weeks (approximately every 28 days, monthly) for the first five injections, followed by 2 mg once every 8 weeks (2 months). Although aflibercept may be dosed as frequently as 2 mg every 4 weeks (approximately every 25 days, monthly), additional efficacy was not demonstrated in most patients when aflibercept was dosed every 4 weeks compared to every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 20 weeks (5 months).
- Diabetic retinopathy: 2 mg via intravitreal injection once every 4 weeks (approximately every 28 days, monthly) for the first five injections, followed by 2 mg once every 8 weeks (2 months). Although aflibercept may be dosed as frequently as 2 mg every 4 weeks (approximately every 25 days, monthly), additional efficacy was not demonstrated in most patients when aflibercept was dosed every 4 weeks compared to every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 20 weeks (5 months).
- Macular edema following retinal vein occlusion: 2 mg via intravitreal injection once every 4 weeks (approximately every 25 days, monthly).
- Neovascular (wet) age-related macular degeneration: 2 mg via intravitreal injection every 4 weeks (approximately every 28 days, monthly) for the first 12 weeks (3 months), followed by 2 mg once every 8 weeks (2 months). Although aflibercept may be dosed as frequently as 2 mg every 4 weeks (approximately every 25 days, monthly), additional efficacy was not demonstrated in most patients when aflibercept was dosed every 4 weeks compared with every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 12 weeks (3 months). Although not as effective as the recommended every

8 week dosing regimen, patients may also be treated with one dose every 12 weeks after one year of effective therapy.
- Retinopathy of prematurity: 0.4 mg via intravitreal injection. Treatment is initiated with a single injection per eligible eye and may be given bilaterally on the same day. Injections may be repeated in each eye; treatment interval between doses injected into the same eye should be at least 10 days.

The recommended dosing for Eylea HD for each indication is as follows:[3]
- Diabetic macular edema: 8 mg via intravitreal injection every 4 weeks (approximately every 28 days, +/- 7 days) for the first three doses, followed by 8 mg once every 8 to 16 weeks, +/- 1 week. Some patients did not maintain a response with extended dosing intervals after successful response to the three initial monthly doses and may benefit from every 4- week dosing (approximately every 28 days, +/- 7 days).
- Diabetic retinopathy: 8 mg via intravitreal injection every 4 weeks (approximately every 28 days, +/- 7 days) for the first three doses, followed by 8 mg once every 8 to 12 weeks, +/- 1 week. Some patients did not maintain a response with extended dosing intervals after successful response to the three initial monthly doses and may benefit from every 4- week dosing (approximately every 28 days, +/- 7 days).
- Macular edema following retinal vein occlusion: 8 mg via intravitreal injection every 4 weeks (approximately every 28 days, +/- 7 days) for the first three to five doses, followed by 8 mg every 8 weeks, ± 1 week. Some patients did not maintain a response with extended dosing intervals after successful response to the first three to five initial monthly doses and may benefit from every 4- week dosing (approximately every 28 days, +/- 7 days).
- Neovascular (wet) age-related macular degeneration: 8 mg via intravitreal injection every 4 weeks (approximately every 28 days, +/- 7 days) for the first three doses, followed by 8 mg once every 8 to 16 weeks, +/- 1 week. Some patients did not maintain a response with extended dosing intervals after successful response to the three initial monthly doses and may benefit from every 4- week dosing (approximately every 28 days, +/- 7 days).

Other Uses with Supportive Evidence for the Aflibercept Products
VEGF is a protein that plays a key role in retinal physiology and pathology.[4] Overexpression of VEGF may result in retinal and choroidal neovascularization and vascular leakage, which can contribute to vision loss associated with common retinal disorders. Intravitreal VEGF inhibitors are highly effective in reducing ocular neovascularization, macular edema, and exudation that can result in vision impairment and/or loss. Intravitreal VEGF inhibitors have been used off-label to manage eye conditions related to increased VEGF production. In addition to the labeled indications for the intravitreal VEGF inhibitors (e.g., neovascular AMD, diabetic macular edema, diabetic retinopathy), examples of other neovascular diseases of the eye that can potentially be treated with intravitreal VEGF inhibitors are angioid streaks, iris neovascularization, neovascular glaucoma, pachychoroid neovasculopathy polypoidal choroidal vasculopathy, and presumed ocular histoplasmosis syndrome. Of note, angioid streaks can occur secondary to systemic conditions such as pseudoxanthoma elasticum, Paget's disease of bone, and sickle cell disease. Research is ongoing and rapidly evolving on the use of intravitreal VEGF inhibitors in other neovascular eye disorders.

Coverage Policy

Policy Statement
Prior Authorization is required for benefit coverage of the intravitreal aflibercept products. Approval is recommended for those who meet the **Criteria and Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests

for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with the intravitreal aflibercept products as well as the monitoring required for adverse events and long-term efficacy, approval requires the intravitreal aflibercept products to be prescribed by or in consultation with a physician who specializes in the condition being treated.

I. Eylea and Pavblu are considered medically necessary when ONE of the following is/are met (1, 2, 3, 4, 5, or 6):

FDA-Approved Indications

1. **Diabetic Macular Edema.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A.** Medication is administered by, or under the supervision of an ophthalmologist; AND
   - **B.** Preferred product criteria is met for the product(s) as listed in the below table(s)

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   - **A)** The dose is 2 mg administered by intravitreal injection for each eye being treated; AND
   - **B)** The dosing interval is not more frequent than once every 25 days for each eye being treated.

2. **Diabetic Retinopathy.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A.** Medication is administered by, or under the supervision of, an ophthalmologist
   - **B.** Preferred product criteria is met for the product(s) as listed in the below table(s)

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   - **A)** The dose is 2 mg administered by intravitreal injection for each eye being treated; AND
   - **B)** The dosing interval is not more frequent than once every 25 days for each eye being treated.

3. **Macular Edema Following Retinal Vein Occlusion.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A.** Medication is administered by, or under the supervision of, an ophthalmologist; AND
   - **B.** Preferred product criteria is met for the products as listed in the below table(s)

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   - **A)** The dose is 2 mg administered by intravitreal injection for each eye being treated; AND
   - **B)** The dosing interval is not more frequent than once every 25 days for each eye being treated.

4. **Neovascular (Wet) Age-Related Macular Degeneration.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A.** Medication is administered by, or under the supervision of, an ophthalmologist; AND

B. Preferred product criteria is met for the products as listed in the below table(s)

Dosing. Approve if the dose meets BOTH of the following (A and B):
A) The dose is 2 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 25 days for each eye being treated.

5. **Retinopathy of Prematurity.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A. Medication is administered by, or under the supervision of, an ophthalmologist; AND
   B. Preferred product criteria is met for the products as listed in the below table(s)

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   A) The dose is 0.4 mg administered by intravitreal injection for each eye being treated; AND
   B) The dosing interval is not more frequent than once every 10 days for each eye being treated.

Other Uses with Supportive Evidence

6. **Other Neovascular Diseases of the Eye.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   Examples of other neovascular diseases of the eye include angioid streaks, iris neovascularization, neovascular glaucoma, pachychoroid neovasculopathy, polypoidal choroidal vasculopathy, and presumed ocular histoplasmosis syndrome.
   A. Medication is administered by, or under the supervision of, an ophthalmologist; AND
   B. Preferred product criteria is met for the products as listed in the below table(s)

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   A) The dose is 2 mg administered by intravitreal injection for each eye being treated; AND
   B) The dosing interval is not more frequent than once every 25 days for each eye being treated.

II. Eylea HD is considered medically necessary when ONE of the following is/are met (1, 2, 3, 4, or 5):

FDA-Approved Indications

1. **Diabetic Macular Edema.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A. Medication is administered by, or under the supervision of, an ophthalmologist; AND
   B. Preferred product criteria is met for the products as listed in the below table(s)

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   A) The dose is 8 mg administered by intravitreal injection for each eye being treated; AND
   B) The dosing interval is not more frequent than once every 21 days for each eye being treated.

Note: The recommended regimen is one dose every 4 weeks (approximately every 28 days +/- 7 day) for the first three doses, followed by one dose every 8 to 16 weeks, +/- 1 week. Some patients may benefit from every 4-week dosing (approximately every 28 days +/- 7 days).

2. **Diabetic Retinopathy.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A.** Medication is administered by, or under the supervision of, an ophthalmologist; AND
   - **B.** Preferred product criteria is met for the products as listed in the below table(s)

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   - **A)** The dose is 8 mg administered by intravitreal injection for each eye being treated; AND
   - **B)** The dosing interval is not more frequent than once every 21 days for each eye being treated.
     Note: The recommended regimen is one dose every 4 weeks (approximately every 28 days +/- 7 day) for the first three doses, followed by one dose every 8 to 12 weeks, +/- 1 week. Some patients may benefit from every 4-week dosing (approximately every 28 days +/- 7 days).

3. **Macular Edema Following Retinal Vein Occlusion.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A.** Medication is administered by, or under the supervision of, an ophthalmologist; AND
   - **B.** Preferred product criteria is met for the products as listed in the below table(s)

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   - **A)** The dose is 8 mg administered by intravitreal injection for each eye being treated; AND
   - **B)** The dosing interval is not more frequent than once every 21 days for each eye being treated.

   Note: The recommended regimen is one dose every 4 weeks (approximately every 28 days +/- 7 day) for the first three to five doses, followed by one dose every 8 weeks, +/- 1 week. Some patients may benefit from every 4-week dosing (approximately every 28 days +/- 7 days.

4. **Neovascular (Wet) Age-Related Macular Degeneration.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A.** Medication is administered by, or under the supervision of, an ophthalmologist; AND
   - **B.** Preferred product criteria is met for the products as listed in the below table(s)

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   - **A)** The dose is 8 mg administered by intravitreal injection for each eye being treated; AND
   - **B)** The dosing interval is not more frequent than once every 21 days for each eye being treated.
     Note: The recommended regimen is one dose every 4 weeks (approximately every 28 days +/- 7 day) for the first three doses, followed by one dose every 8 to 16 weeks, +/- 1 week. Some patients may benefit from every 4-week dosing (approximately every 28 days +/- 7 days).

Other Uses with Supportive Evidence

5. **Other Neovascular Diseases of the Eye.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Medication is administered by or under the supervision of an ophthalmologist; AND
   B) Preferred product criteria is met for the product(s) as listed in the below table(s)
   Note: Examples of other neovascular diseases of the eye include angioid streaks, iris neovascularization, neovascular glaucoma, pachychoroid neovasculopathy, polypoidal choroidal vasculopathy, and presumed ocular histoplasmosis syndrome.

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   A) The dose is 8 mg administered by intravitreal injection for each eye being treated; AND
   B) The dosing interval is not more frequent than once every 21 days for each eye being treated.

Employer Plans:

Product	Criteria
Eylea (aflibercept intravitreal injection) **Eylea HD** (aflibercept intravitreal injection) **Pavblu** (aflibercept-ayyh intravitreal injection)	Patient meets **ONE** of the following (i or ii): **i.** Patient is currently receiving Eylea HD, Eylea, or Pavblu; OR **ii.** Patient meets **ONE** of the following (a, b, c, d, e or f): **a.** Patient meets **BOTH** of the following (1 and 2): **1.** Patient has previously tried repackaged bevacizumab; AND **2.** Either inadequate efficacy or intolerability was demonstrated; OR **b.** According to the prescriber, patient has diabetic macular edema and a baseline Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA) of 20/50 or worse (< 69 ETDRS letters); OR **c.** According to the prescriber, patient has diabetic macular edema with significant retinal thickening; OR **d.** Patient has diabetic retinopathy (without diabetic macular edema); OR **e.** In the professional opinion of the prescriber, the safety of using the repackaged bevacizumab is of significant concern; OR **f.** In the professional opinion of the prescriber, the supplier of the repackaged bevacizumab is of significant concern.

Individual and Family Plans:

Product	Criteria
Eylea (aflibercept intravitreal injection)	Patient meets **ONE** of the following (i or ii): **i.** Patient is currently receiving Eylea HD, Eylea, or Pavblu; OR **ii.** Patient meets **ONE** of the following (a, b, c, d, e or f): **a.** Patient meets **BOTH** of the following (1 and 2): **1.** Patient has previously tried repackaged bevacizumab; AND

Product	Criteria
Eylea HD (aflibercept intravitreal injection) **Pavblu** (aflibercept-ayyh intravitreal injection)	**2.** Either inadequate efficacy or intolerability was demonstrated; OR **b.** According to the prescriber, patient has diabetic macular edema and a baseline Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA) of 20/50 or worse (< 69 ETDRS letters); OR **c.** According to the prescriber, patient has diabetic macular edema with significant retinal thickening; OR **d.** Patient has diabetic retinopathy (without diabetic macular edema); OR **e.** In the professional opinion of the prescriber, the safety of using the repackaged bevacizumab is of significant concern; OR **f.** In the professional opinion of the prescriber, the supplier of the repackaged bevacizumab is of significant concern.

Conditions Not Covered

Eylea, Eylea HD, Pavblu for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent Use with Another Intravitreal Vascular Endothelial Growth Factor Inhibitor.** There is no evidence to support concomitant use of intravitreal aflibercept injection (Eylea, Pavblu, and Eylea HD) with another intravitreal vascular endothelial growth factor inhibitor.
   Note: Intravitreal vascular endothelial growth factor inhibitors are: bevacizumab intravitreal injection (compounded from Avastin® [bevacizumab, injection, for intravenous use] or itsbiosimilars; off-label use), Beovu® (brolucizumab-dbll intravitreal injection), ranibizumab intravitreal injection (Lucentis®, biosimilars), Susvimo® (ranibizumab intravitreal injection via ocular implant), and Vabysmo® (faricimab-svoa intravitreal injection).

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals (Code effective until 3/31/2025)
J0177	Injection, aflibercept HD, 1 mg (Code effective 4/1/2024)
J0178	Injection, aflibercept, 1 mg
J3490	Unclassified drugs (Code effective until 3/31/2025)
J3590	Unclassified biologics (Code effective until 3/31/2025)
Q5147	Injection, aflibercept-ayyh (Pavblu), biosimilar, 1 mg (Code effective 4/1/2025)

References

1. Eylea® intravitreal injection [prescribing information]. Tarrytown, NY: Regeneron; October 2024.
2. Pavblu™ intravitreal injection [prescribing information]. Thousand Oaks, CA: Amgen; August 2024.
3. Eylea® HD intravitreal injection [prescribing information]. Tarrytown, NY: Regeneron; November 2025.
4. Hang A, Feldman S, Amin AP, et al. Intravitreal anti-vascular endothelial growth factor therapies for retinal disorders. *Pharmaceuticals*. 2023;16:1140. Doi.org/10.3390/ph16081140.

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	**Updated** review date, disclaimer, refreshed background, and references, and added change history. **Eylea, Eylea HD:** For the exclusion criterion "Patient has diabetic macular edema and a baseline visual acuity worse than 20/40", the threshold was rephrased as "20/50 or worse (< 69 Early Treatment Diabetic Retinopathy Study [ETDRS] letters)" to align with the language used in the study. In addition, baseline visual acuity was clarified as "ETDRS best-corrected visual acuity (BCVA)." **Updated Coding:** **Removed** J3590 **Added** J0177 (effective 4/1/2024)	12/01/2024
Selected Revision	**Pavblu:** Pavblu (biosimilar to Eylea) was added to the policy; conditions and criteria for approval for Pavblu are identical to those for Eylea. **Preferred Product Table:** **Updated** criteria **from** "Diabetic retinopathy **to** "Diabetic retinopathy (without diabetic macular edema) for Eylea and Eylea HD." **Added** preferred product step requirement for Pavblu. **Updated HCPCS Coding:** **Added:** C9399, J3490, J3590	02/01/2025
Selected Revision	**Updated HCPCS Coding** **Added** new code Q5147 that will be effective on 4/1/2025 **Added** that C9399, J3490 & J3590 will be effective until 3/31/2025	03/15/2025

Selected Revision	**Employer Plans and Individual and Family Plans Preferred Product Criteria Tables. Updated** criteria language.	09/15/2025
Annual Revision	Policy title updated from "Aflibercept " to "Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Aflibercept Products" **Added** a policy statement. **Eylea, Pavblu: Other Uses with Supportive Evidence.** Other Neovascular Diseases of the Eye. The Note of examples of other neovascular diseases was revised to remove sickle cell neovascularization and choroidal neovascular conditions and the following examples were added: angioid streaks, iris neovascularization, pachychoroid neovasculopathy, polypoidal choroidal vasculopathy, and presumed ocular histoplasmosis. **Eylea HD: Other Uses with Supportive Evidence.** Added **"**Other Neovascular Diseases of the Eye" as a condition of approval. **Eylea HD: Dosing.** A note, defining the recommended dosing was added to the dosing for each indication. **Conditions Not Covered:** "Concomitant Use with Another Intravitreal Vascular Endothelial Growth Factor Inhibitor" was added. **Eylea HD, Macular Edema Following Retinal Vein Occlusion:** This condition of approval was added to the policy. Dosing recommendation for this condition was also added. Eylea HD, Dosing section was revised to align with the updated Eylea HD prescribing information (PI). **Diabetic Macular Edema:** The dosing interval was revised to read "not more frequent than once every 21 days for each eye being treated"; previously the dosing interval was "not more frequent than once every 21 days for the first three doses, followed by not more frequent that once every 7 weeks for each eye being treated". The revised PI notes that some patients may benefit from every 4-week dosing (approximately every 28 days, +/- 7 days). **Diabetic Retinopathy:** The dosing interval was revised to read "not more frequent than once every 21 days for each eye being treated"; previously the dosing interval was "not more frequent than once	02/01/2026

	every 21 days for the first three doses, followed by not more frequent that once every 7 weeks for each eye being treated". The revised PI notes that some patients may benefit from every 4-week dosing (approximately every 28 days, +/- 7 days). **Neovascular (Wet) Age-Related Macular Degeneration:** The dosing interval was revised to read "not more frequent than once every 21 days for each eye being treated"; previously the dosing interval was "not more frequent than once every 21 days for the first three doses, followed by not more frequent that once every 7 weeks for each eye being treated". The revised PI notes that some patients may benefit from every 4-week dosing (approximately every 28 days, +/- 7 days). **Added** preferred product requirements.	

The policy effective date is in force until updated or retired.