Utilization Review Policy 267A

POLICY: Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Aflibercept Products Utilization Management Medical Policy

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

EFFECTIVE DATE: 1/1/2022
LAST REVISION DATE: 10/15/2025; selected revision 12/10/2025

COVERAGE CRITERIA FOR: UCare Medical Assistance and Exchange Plans Only (PMAP, Connect, MSC+, MnCare, all Individual and Family Plans)

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.

POLICY STATEMENT

Prior Authorization is recommended for medical 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Eylea, Eylea HD and Pavblu is recommended for requests meeting both the step therapy requirements and indication requirements:

Step Therapy Requirements (New Starts Only)

Criteria. *The patient must meet the following criteria (A, B, C, D, or E):*

A) For patients new to Eylea, Eylea HD or Pavblu therapy only, must have a trial of repackaged Avastin prior to approval of Eylea, Eylea HD or Pavblu. New starts to therapy defined as no use of Eylea, Eylea HD or Pavblu within the past 180 days for Medicaid and Commercial patients and includes use in either eye.

B) Patient has diabetic macular edema and has a baseline visual acuity worse than 20/40 according to the prescriber

C) Patient has diabetic macular edema with significant retinal thickening according to the prescriber;

D) Patient has diabetic retinopathy (without diabetic macular edema)

E) Patient has a contraindication or other clinical reason why repackaged Avastin cannot be tried before Eylea, Eylea HD or Pavblu.

Note: Step therapy only required for indications compendia supported for both Eylea, Eylea HD, Pavblu and Avastin.

RECOMMENDED AUTHORIZATION CRITERIA

I. Coverage of Eylea and Pavblu is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Diabetic Macular Edema. Approve for 1 year if administered by or under the supervision of an ophthalmologist.

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 administered by or under the supervision of an ophthalmologist.

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 administered by or under the supervision of an ophthalmologist.

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 administered by or under the supervision of an ophthalmologist.

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 administered by or under the supervision of an ophthalmologist.

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 administered by or under the supervision of an ophthalmologist.
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 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. Coverage of Eylea HD is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Diabetic Macular Edema. Approve for 1 year if administered by or under the supervision of an ophthalmologist.

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).

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2. Diabetic Retinopathy. Approve for 1 year if administered by or under the supervision of an ophthalmologist.

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).

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3. Macular Edema Following Retinal Vein Occlusion. Approve for 1 year if administered by or under the supervision of an ophthalmologist.

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.

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4. Neovascular (Wet) Age-Related Macular Degeneration. Approve for 1 year if administered by or under the supervision of an ophthalmologist.

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 administered by or under the supervision of an ophthalmologist.
   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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of the intravitreal aflibercept products is not recommended in the following situations:

1. **Concomitant 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 its biosimilars; 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).

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	11/14/2018
Selected Revision	For Eylea, the condition, Diabetic retinopathy in patients with Diabetic Macular Edema, was update to include all patients with Diabetic Retinopathy. Previously the product was only indicated to treatment Diabetic Retinopathy in patients who also had DME.	5/22/2019
Annual Revision	The dosing in the approval conditions for **Neovascular (Wet) Age-Related Macular Degeneration, Macular Edema Following Retinal Vein Occlusion, Diabetic Macular Edema, Diabetic Retinopathy, and Other Neovascular Ophthalmic Conditions** was changed from "the dose is 2 mg" to "The dose is ≤ 2 mg".	11/06/2019
Annual Revision	No criteria changes.	11/04/2020

Annual Revision	**Diabetic Macular Edema, Diabetic Retinopathy, Macular Edema following Retinal Vein Occlusion,** and **Neovascular (wet) Aage-Related Macular Degeneration:** To align with the FDA-approved dosing, the dose was changed from "≤ 2 mg" to "is 2 mg". **Other Neovascular Diseases of the Eye:** Examples of other neovascular diseases of the eye were moved to a Note. To align with the FDA-approved dosing, the dose was changed from "≤ 2 mg" to "is 2 mg".	11/10/2021
UCare Revision	Clarified that continuation of therapy is acceptable if the requested product has been used in either eye.	10/7/2022
Selected Revision	**Retinopathy of Prematurity:** This condition was moved to the FDA-Approved Indications; previously, it was included in the Note of examples of Other Neovascular Diseases of the Eye, under "Other Uses with Supportive Evidence". For this indication, the dosing was changed to be 0.4 mg administered per injection, with the dosing interval changed to be not more frequent than once every 10 days for each eye being treated (previously, it was the same as Other Neovascular Diseases of the Eye, which was 2 mg per treated eye, with a dosing interval of at least 25 days between doses).	02/22/2023
Selected Revision	**Eylea HD:** Eylea HD was added to the policy; conditions and criteria for approval were added to the policy.	08/30/2023
Annual Revision	No criteria changes.	11/15/2023
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
Annual Revision	**Pavblu:** Pavblu (biosimilar to Eylea) was added to the policy; conditions and criteria for approval for Pavblu are identical to those for Eylea. **Policy name:** Policy name was changed from Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Eylea and Eylea HD to Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Aflibercept Products.	01/06/2025
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/15/2025
Annual Revision	**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. **Conditions Not Recommended for Approval.** "Concomitant Use with Another Intravitreal Vascular Endothelial Growth Factor Inhibitor" was added.	10/15/2025