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: 01/06/2025

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, Eylea HD, and Pavblu, are given intravitreally for the treatment of ophthalmic conditions. Pavblu is a biosimilar to Eylea.[3]

Eylea and Pavblu are indicated for the following uses:[1-3]

- **Diabetic macular edema**.
- **Diabetic retinopathy**.
- **Macular edema following retinal vein occlusion**.
- **Neovascular (wet) age-related macular degeneration**.

Eylea is also indicated for the treatment of **retinopathy of prematurity**.[1]

Eylea HD, a high dose aflibercept product, is indicated for the following uses:[6]

- **Diabetic macular edema**.
- **Diabetic retinopathy**.
- **Neovascular (wet) age-related macular degeneration**.

Dosing Information:

The recommended dosing for Eylea and Pavblu for each indication is as follows:

- Diabetic macular edema or 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 Eylea/Pavblu 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 Eylea/Pavblu 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 every 8 weeks (2 months). Although Eylea/Pavblu 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 Eylea/Pavblu 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 (Eylea only): 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:

- 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.
- 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.
- 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.

Other Uses with Supportive Evidence for Eylea and Pavblu

Overproduction of VEGF may lead to other eye conditions, including neovascular glaucoma and other retinal and choroidal neovascular conditions affecting the eye.[4,5] The VEGF inhibitors have the potential to be used off-label to reduce or slow visual impairment or vision loss associated with other eye conditions related to increased VEGF production.[4,6,7] The use of VEGF inhibitors have been shown to stop the angiogenic process, maintain visual acuity, and improve vision in patients with certain neovascular ophthalmic conditions. Therefore, research is rapidly evolving on the use of VEGF inhibitors in other neovascular ophthalmic conditions that threaten vision.[6,7]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of the intravitreal aflibercept products (Eylea, Eylea HD, and Pavblu). 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.

FDA-Approved Indications

---

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 neovascular glaucoma, sickle cell neovascularization, and choroidal neovascular conditions.

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.

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

FDA-Approved Indications

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 three doses, followed by not more frequent than once every 7 weeks for each eye being treated.
Note: The recommended dose is once 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.

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 three doses, followed by not more frequent than once every 7 weeks for each eye being treated.
Note: The recommended dose is once 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.

3. 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 three doses, followed by not more frequent than once every 7 weeks for each eye being treated.
Note: The recommended dose is once 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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

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

1. 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; December 2023.
2. Eylea® HD intravitreal injection [prescribing information]. Tarrytown, NY: Regeneron; December 2023.
3. Pavblu™ intravitreal injection [prescribing information]. Thousand Oaks, CA: Amgen; August 2024.
4. Barakat MR, Kaiser PK. VEGF inhibitors for the treatment of neovascular age-related macular degeneration. *Expert Opin Investig Drugs.* 2009;18(5):637-646.
5. Tolentino M. Systemic and ocular safety of intravitreal anti-VEGF therapies for ocular neovascular disease. *Surv Ophthalmol*. 2011;56(2):95-113.
6. Kinnunen K, Ylä-Herttuala S. Vascular endothelial growth factors in retinal and choroidal neovascular diseases. *Ann Med.* 2012;44(1):1-17.
7. Horsley MB, Kahook MY. Anti-VEGF therapy for glaucoma. *Curr Opin Ophthalmol*. 2010;21(2):112-117.

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