UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Aflibercept Products Utilization Management Medical Policy
- Eylea® (aflibercept intravitreal injection – Regeneron)
- Eylea® HD (aflibercept intravitreal injection – Regeneron)
- Pavblu™ (aflibercept-ayyh intravitreal injection – Amgen)
- Yesafili™ (aflibercept-jbvf intravitreal injection – Biocon Biologics)

REVIEW DATE: 10/15/2025; selected revision 12/10/2025, 06/10/2026, 07/22/2026

OVERVIEW

Aflibercept is a vascular endothelial growth factor (VEGF) inhibitor.[1-3,5] Ophthalmic aflibercept products (Eylea and its biosimilars and Eylea HD) are given intravitreally for the treatment of ophthalmic conditions. Pavblu and Yesafili are biosimilars 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/biosimilars) is indicated for the following uses:[1,2.5]
- **Diabetic macular edema**.
- **Diabetic retinopathy**.
- **Macular edema following retinal vein occlusion (RVO)**.
- **Neovascular (wet) age-related macular degeneration (AMD)**.
- **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 RVO.**
- **Neovascular (wet) AMD**.

Dosing Information:

The recommended dosing for aflibercept (Eylea/biosimilars) for each indication is as follows:[1,2,5]
- 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 RVO: 2 mg via intravitreal injection once every 4 weeks (approximately every 25 days, monthly).

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- Neovascular (wet) AMD: 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 resuming every 4-week dosing (approximately every 28 days, ± 7 days). Extended dosing intervals (8 mg once every 20 weeks, ± 1 week) may be considered after 1 year of successful response based on visual and anatomic outcomes.
- 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 resuming every 4-week dosing (approximately every 28 days, ± 7 days).
- Macular edema following RVO: 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 resuming every 4- week dosing (approximately every 28 days, ± 7 days).
- Neovascular (wet) AMD: 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 resuming every 4- week dosing (approximately every 28 days, ± 7 days). Extended dosing intervals (8 mg once every 20 weeks, ± 1 week) may be considered after 1 year of successful response based on visual and anatomic outcomes.

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

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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

I. Coverage of Eylea and its biosimilars (Pavblu and Yesafili) 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.

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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 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.

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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 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.

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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 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.

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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

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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.

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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.

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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.

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.

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.

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REFERENCES

1. Eylea® intravitreal injection [prescribing information]. Tarrytown, NY: Regeneron; October 2024.
2. Pavblu™ intravitreal injection [prescribing information]. Thousand Oaks, CA: Amgen; April 2026.
3. Eylea® HD intravitreal injection [prescribing information]. Tarrytown, NY: Regeneron; April 2026.
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.
5. Yesafili™ intravitreal injection [prescribing information]. Cambridge, MA: Biocon Biologics; May 2024

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/15/2023
Annual Revision	**Pavblu:** Pavblu (biosimilar to Eylea) was added to the policy; conditions and requirements 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.	10/30/2024
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
Selected Revision	**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 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).	12/10/2025
Selected Revision	**Eylea HD – Diabetic Macular Edema, Diabetic Retinopathy, Macular Edema Following Retin Vein Occlusion, and Neovascular (Wet) Age-Related Macular Degeneration):** The Note regarding the recommended dose for Eylea HD was removed from the Dosing section.	06/10/2026
Selected Revision	**Yesafili:** Yesafili (biosimilar to Eylea) was added to the policy; conditions and requirements for approval for Yesafili are identical to those for Eylea.	07/22/2026

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