

Medicare Advantage Medical Utilization Review Policy

Policy:	Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Aflibercept Products Utilization Management Medical Policy <ul style="list-style-type: none"> • Eylea® (aflibercept intravitreal injection – Regeneron) • Eylea® HD (aflibercept intravitreal injection – Regeneron) • Pavblu™ (aflibercept-ayyh intravitreal injection – Amgen)
Date:	12/02/2024
Applicable Lines of Business:	Medicare Advantage - Medical
Applicable States:	NGS, J6: Wisconsin, Minnesota, Illinois NGS, JK: New York, Connecticut, Massachusetts, Maine, New Hampshire, Rhode Island, Vermont

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 indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. All approvals are provided for the duration noted below.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.



Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. Neovascular (Wet) Age-Related Macular Degeneration.

Criteria. Approve for 1 year.

Dosing. Approve if the requested dosing meets 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. Macular Edema Following Retinal Vein Occlusion.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both criteria (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. Diabetic Macular Edema.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both criteria (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. Diabetic Retinopathy.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both criteria (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.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both of the following criteria (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.

Note: Examples of other neovascular diseases of the eye include neovascular glaucoma, sickle cell neovascularization, choroidal neovascular conditions.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both criteria (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

1. Diabetic Macular Edema.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both of the following (A and B):

- C) The dose is 8 mg administered by intravitreal injection for each eye being treated; AND
- D) 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.

Criteria. Approve for 1 year.

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.

Criteria. Approve for 1 year.

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.
8. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Determination (LCD): Drugs and Biologicals, Coverage of, for Label and Off-Label Uses (L33394) [original date 10/01/2015; revision effective date 8/1/24]. Accessed December 2, 2024.
9. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Article (LCA): Billing and Coding: Ranibizumab, Aflibercept and Brolucizumab-dblb (A52451) [original date 10/01/2015; revision effective date 9/1/24]. Accessed December 2, 2024.

HISTORY

Type of Revision	Summary of Changes*	Date
Policy created	New Medicare Advantage Medical Policy	07/11/2018
Policy revision	Added Macugen to policy	11/05/2018
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52451 and Ophthalmology	5/22/2019



	– Vascular Endothelial Growth Factor (VEGF) Inhibitor Injectables Utilization Review Policy.	
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Determination L33394 and Ophthalmology – Vascular Endothelial Growth Factor Inhibitors - Eylea Utilization Review Policy.	11/06/2019
Policy revision	Non-clinical update to policy to add the statement “This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does <u>not</u> necessarily mean that the applicable condition or diagnosis is excluded from coverage.”	1/30/2020
Policy revision	*Added the following to the Policy Statement “ <u>Note</u> : Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.” *Updated references	08/07/2020
Policy revision	Diabetic Macular Edema, Diabetic Retinopathy, Macular Edema following Retinal Vein Occlusion, and Neovascular (wet) Age-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”.	12/20/2021
Policy 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).	03/08/2023
Policy revision	Eylea HD: Eylea HD was added to the policy; conditions and criteria for approval were added to the policy.	09/26/2023
Policy review	No criteria changes, review based on LCD/LCA update.	09/11/2024
Policy revision	Pavblu: Pavblu (biosimilar to Eylea) was added to the policy; conditions and criteria for approval for Pavblu are identical to those for Eylea.	12/02/2024



	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.	
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