Medicare Advantage Medical Utilization Review Policy

Policy:	**Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Eylea and Eylea HD Utilization Management Medical Policy** • Eylea® (aflibercept intravitreal injection – Regeneron) • Eylea® HD (aflibercept intravitreal injection – Regeneron)
Date:	09/26/2023
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

Eylea, a vascular endothelial growth factor (VEGF) inhibitor, is indicated for the following uses:[1]

- **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 VEGF inhibitor, is indicated for the following uses:[6]

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

For all of the indications, except retinopathy of prematurity, the recommended dose for Eylea is 2 mg administered by intravitreal injection. Frequency of the dose varies depending on the condition, although all conditions state some patients may need upper limit dosing of once every 4 weeks (approximately every 25 days, monthly). The dose for retinopathy of prematurity is 0.4 mg administered by intravitreal injection; repeat injections may be given and the treatment interval between doses injected into the same eye should be at least 10 days.

For all indications, the recommended dose for Eylea HD is 8mg administered by intravitreal injection.[6] For diabetic macular edema and neovascular (wet) age-related macular degeneration, the dosing regimen for Eylea HD is 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. For diabetic retinopathy, the dosing is 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.

Other Uses with Supportive Evidence for Eylea

Overproduction of VEGF may lead to other eye conditions, including neovascular glaucoma and other retinal and choroidal neovascular conditions affecting the eye.[2,3] Thus, the VEGF inhibitors have the potential to be used off-label for the treatment of other neovascular diseases of the eye to prevent or reduce vision loss .[2,4,5] The use of anti-VEGF agents have been shown to stop the angiogenic process and 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 which threaten vision.[4,5]

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Eylea and Eylea HD. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). 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 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.

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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.

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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.

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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

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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 Eylea and Eylea HD 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; February 2023.
2. Barakat MR, Kaiser PK. VEGF inhibitors for the treatment of neovascular age-related macular degeneration. *Expert Opin Investig Drugs*. 2009;18(5):637-646.

3. Tolentino M. Systemic and ocular safety of intravitreal anti-VEGF therapies for ocular neovascular disease. *Surv Ophthalmol*. 2011;56(2):95-113.
4. Kinnunen K, Ylä-Herttuala S. Vascular endothelial growth factors in retinal and choroidal neovascular diseases. *Ann Med*. 2012;44(1):1-17.
5. Horsley MB, Kahook MY. Anti-VEGF therapy for glaucoma. *Curr Opin Ophthalmol*. 2010;21(2):112-117.
6. Eylea® HD intravitreal injection [prescribing information]. Tarrytown, NY: Regeneron; August 2023.
7. 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 11/1/2022]. Accessed on September 26, 2023.
8. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Article (LCA): Billing and Coding: Ranibizumab, Aflibercept and Brolucizumab-dbll (A52451) [original date 10/01/2015; revision effective date 4/1/2023]. Accessed on September 26, 2023.

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 – Vascular Endothelial Growth Factor (VEGF) Inhibitor Injectables Utilization Review Policy.	5/22/2019
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 not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020
Policy revision	*Added the following to the Policy Statement "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." *Updated references	08/07/2020
Policy 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".	12/20/2021

	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".	
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