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Coverage Policy Number **IP0540**

Aflibercept

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following aflibercept products:

- **Eylea®** (aflibercept intravitreal injection)
- **Eylea® HD** (aflibercept intravitreal injection)

Additional criteria that support the review for medical necessity exceptions of non-preferred products are located in the Non-Preferred Product Table by the respective plan type and drug list where applicable.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Aflibercept products (Eylea and Eylea HD) are considered medically necessary when ONE of the following are met:

I. **Aflibercept (Eylea).** Individual meets **ALL** of the following criteria:

1. Treatment of **ONE** of the following
    A. Diabetic Macular Edema (DME)
    B. Diabetic Retinopathy (DR)
    C. Macular Edema following retinal vein occlusion (RVO)
    D. Neovascular (wet) Age-Related Macular Degeneration
    E. Retinopathy of Prematurity
    F. Other Neovascular Diseases of the Eye (for example, neovascular glaucoma, sickle cell neovascularization, choroidal neovascular conditions)
2. Medication is prescribed by, or under the supervision of, an ophthalmologist
3. Non-Preferred Product Criteria is met, refer to below table(s)

Dosing. ONE of the following dosing regimens:[1]

1. For ALL covered diagnoses (except retinopathy of prematurity), **BOTH** of the following:
    A. 2 mg administered by intravitreal injection for each eye being treated
    B. The dosing interval is not more frequent than once every 25 days for each eye being treated
2. For retinopathy of prematurity, **BOTH** of the following:
    A. 0.4 mg administered by intravitreal injection for each eye being treated
    B. The dosing interval is not more frequent than once every 10 days for each eye being treated

Employer Group Non-Preferred Products and Criteria:

Non-Preferred Product	Criteria
Eylea (aflibercept intravitreal injection)	Documentation of **ONE** of the following: 1. Currently receiving Eylea 2. **ONE** of the following: A. Failure, contraindication, or intolerance to repackaged bevacizumab B. If, in the professional opinion of the prescriber, the safety of using the repackaged bevacizumab or the supplier of the repackaged bevacizumab is of significant concern 3. Diabetic macular edema with a baseline visual acuity worse than 20/40 4. Diabetic macular edema with significant retinal thickening 5. Diabetic retinopathy

Individual and Family Plan Non-Preferred Products and Criteria:

Non-Preferred Product	Criteria
Eylea (aflibercept intravitreal injection)	Documentation of **ONE** of the following: 1. Currently receiving Eylea 2. **ONE** of the following: A. Failure, contraindication, or intolerance to repackaged bevacizumab B. If, in the professional opinion of the prescriber, the safety of using the repackaged bevacizumab or the supplier of the repackaged bevacizumab is of significant concern 3. Diabetic macular edema with a baseline visual acuity worse than 20/40 4. Diabetic macular edema with significant retinal thickening

Non-Preferred Product	Criteria
	5. Diabetic retinopathy

II. **Aflibercept (Eylea HD).** Individual meets **ALL** of the following criteria:

1. Treatment of **ONE** of the following
   A. Diabetic Macular Edema (DME)
   B. Diabetic Retinopathy (DR)
   C. Neovascular (wet) Age-Related Macular Degeneration
2. Medication is prescribed by, or under the supervision of, an ophthalmologist
3. Non-Preferred Product Criteria is met, refer to below table(s)

Dosing. For ALL covered diagnoses, **BOTH** of the following:[6]
1. 8 mg administered by intravitreal injection for each eye being treated
2. 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

Employer Group Non-Preferred Products and Criteria:

Non-Preferred Product	Criteria
Eylea HD (aflibercept intravitreal injection)	Documentation of **ONE** of the following: 1. Currently receiving Eylea HD 2. **ONE** of the following: A. Failure, contraindication, or intolerance to repackaged bevacizumab B. If, in the professional opinion of the prescriber, the safety of using the repackaged bevacizumab or the supplier of the repackaged bevacizumab is of significant concern 3. Diabetic macular edema with a baseline visual acuity worse than 20/40 4. Diabetic macular edema with significant retinal thickening 5. Diabetic retinopathy

Individual and Family Plan Non-Preferred Products and Criteria:

Non-Preferred Product	Criteria
Eylea HD (aflibercept intravitreal injection)	Documentation of **ONE** of the following: 1. Currently receiving Eylea HD 2. **ONE** of the following: A. Failure, contraindication, or intolerance to repackaged bevacizumab B. If, in the professional opinion of the prescriber, the safety of using the repackaged bevacizumab or the supplier of the repackaged bevacizumab is of significant concern 3. Diabetic macular edema with a baseline visual acuity worse than 20/40 4. Diabetic macular edema with significant retinal thickening 5. Diabetic retinopathy

Non-Preferred Product	Criteria

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of aflibercept (Eylea and Eylea HD) is considered medically necessary for ALL covered diagnoses when the above medical necessity criteria are met AND beneficial response is demonstrated.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J0178	Injection, aflibercept, 1 mg
J3590	Unclassified biologics

Background

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] The dosing interval of Eylea HD is every 4 weeks (approximately every 28 days +/- 7 day) for the first three doses, followed by one dose very 8 to 16 weeks, +/- 1 week.

Other Uses with Supportive Evidence
Overproduction of VEGF may lead to other eye conditions, including neovascular glaucoma and other retinal and choroidal neovascular conditions affecting the eye.[2,3] The VEGF inhibitors also have the potential to be used off-label in other eye conditions 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]

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.