Clinical Policy: Aflibercept (Eylea)

Reference Number: ERX.SPA.203
Effective Date: 01.11.17
Last Review Date: 02.18 Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Aflibercept (Eylea®) is a vascular endothelial growth factor (VEGF) inhibitor.

FDA Approved Indication(s)
Eylea is indicated for the treatment of patients with:
- Neovascular (wet) age-related macular degeneration (AMD)
- Macular edema following retinal vein occlusion (RVO)
- Diabetic macular edema (DME)
- Diabetic retinopathy (DR) in patients with DME

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Eylea is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Ophthalmic Disease (must meet all)**:**

1. Diagnosis of one of the following (a, b, c, or d):
   a. Neovascular (wet) AMD;
   b. Macular edema following RVO;
   c. DME;
   d. DR in the presence of DME;
2. Prescribed by or in consultation with an ophthalmologist;
3. Age ≥ 18 years;
4. For all indications except for DME in members with baseline visual acuity worse than 20/50: Failure of a trial of bevacizumab unless contraindicated or clinically significant adverse effects are experienced;
5. Eylea is not prescribed concurrently with other anti-vascular endothelial growth factor (VEGF) medications;
6. Dose does not exceed:
   a. AMD: 2 mg (1 vial) via intravitreal injection every 4 weeks for the first 3 months, then every 8 weeks thereafter;
   b. DME and DR in the presence of DME: 2 mg (1 vial) via intravitreal injection every 4 weeks for the first 5 injections, then every 8 weeks thereafter;
   c. RVO: 2 mg (1 vial) via intravitreal injection every 4 weeks.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Ophthalmic Disease (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;

2. Member is responding positively to therapy as evidenced by one of the following (a, b, c, or d):
   a. Detained neovascularization;
   b. Improvement/stabilization in visual acuity;
   c. Maintenance of corrected visual acuity from prior treatment;
   d. Supportive findings from optical coherence tomography or fluorescein angiography;
3. Eylea is not prescribed concurrently with other anti-VEGF medications;
4. If request is for a dose increase, new dose does not exceed:
   a. AMD, DME, and DR in the presence of DME: 2 mg (1 vial) via intravitreal injection every 8 weeks;
   b. RVO: 2 mg (1 vial) via intravitreal injection every 4 weeks.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
AMD: age-related macular degeneration
DME: diabetic macular edema
DR: diabetic retinopathy
FDA: Food and Drug Administration
RVO: retinal vein occlusion
VEGF: vascular endothelial growth factor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Avastin® (bevacizumab)	**Neovascular (wet) AMD:** 1.25 to 2.5 mg administered by intravitreal injection every 4 weeks.	2.5 mg/month
	Macular edema secondary to RVO: 1 mg to 2.5 mg administered by intravitreal injection every 4 weeks	2.5 mg/month
	DR: 1.25 mg administered by intravitreal injection every 6 weeks	1.25 mg/6 weeks
	DME: 1.25 mg administered by intravitreal injection every 6 weeks	1.25 mg/6 weeks

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: General Information

- In the VEGF Trap-Eye: Investigation of Efficacy and Safety in Wet Age-Related Macular Degeneration (VIEW)-1 trial, the difference in the number of patients who lost fewer than 15 letters at 52 weeks between Eylea every 8 weeks compared to Lucentis was 0.6% (95.1% CI -0.32, 4.4). In terms of the number of patients who gained at least 15 letters, the mean difference

between Eylea every 8 weeks was 6.6% (95.1% CI -1.0, 14.1). There were no adverse events that were found to be significant from the Lucentis arm.

- In a trial comparing Eylea, Avastin and Lucentis, the Diabetic Retinopathy Clinical Research Network found in patients with diabetic macular edema that when the initial visual-acuity letter score was 78 to 69 (equivalent to approximately 20/32 to 20/40) (51% of participants), the mean improvement was 8.0 with Eylea, 7.5 with Avastin, and 8.3 with Lucentis ($p > 0.50$ for each pair wise comparison). When the initial letter score was less than 69 (approximately 20/50 or worse), the mean improvement was 18.9 with Eylea, 11.8 with Avastin, and 14.2 with Lucentis ($p < 0.001$ for Eylea vs. Avastin, $p = 0.003$ for Eylea vs. Lucentis, and $p = 0.21$ for Lucentis vs. Avastin).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AMD	2 mg (1 vial) administered by intravitreal injection once a month for 3 months then 2 mg every 2 months *Although Eylea may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated in most patients when Eylea was dosed every 4 weeks compared to every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 12 weeks (3 months).*	2 mg/month
Macular edema following RVO	2 mg (1 vial) administered by intravitreal injection once every 4 weeks (monthly)	2 mg/month
DME and DR with DME	2 mg (1 vial) administered by intravitreal injection once a month for the first 5 injections followed by 2 mg via intravitreal injection once every 2 months *Although Eylea may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated in most patients when Eylea 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).*	2 mg/month

VI. Product Availability

Single-use vial: 40 mg/mL solution in a 0.05 mL total volume

VII. References

1. Eylea Prescribing Information. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; May 2017. Available at: www.eylea.com. Accessed November 10, 2017.
2. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; January 2015. Available at www.aao.org/ppp. Accessed November 10, 2017.
3. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; November 2015. Available at www.aao.org/ppp. Accessed November 10, 2017.
4. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; February 2016. Available at www.aao.org/ppp. Accessed November 10, 2017.
5. Wells JA, Glassman AR, Ayala AR, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. N Engl J Med. 2015 Mar 26;372(13):1193-203. doi: 10.1056/NEJMoa1414264

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	12.16	01.17
1Q18 annual review: Converted to new template.	11.23.17	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added bevacizumab redirection except for members with baseline visual acuity worse than 20/50 due to clinical superiority of Eylea Added specialist requirement Removed criteria checking for contraindications (ocular infections) due to its ophthalmic nature and addition of specialist requirement Added age limit		

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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