Aflibercept

NDC CODE(S) 61755-0005-XX EYLEA 2MG/0.05ML Solution (REGENERON PHARMACEUTICALS)

DESCRIPTION

Aflibercept is a recombinant fusion protein consisting of portions of human VEGF receptors 1 and 2 extracellular domains fused to the Fc portion of human IgG1 formulated as an iso-osmotic solution for intravitreal administration. Vascular endothelial growth factor-A (VEGF-A) and placental growth factor (PlGF) are members of the VEGF family of angiogenic factors that can act as mitogenic, chemotactic, and vascular permeability factors for endothelial cells.

VEGF acts via two receptor tyrosine kinases, VEGFR-1 and VEGFR-2, present on the surface of endothelial cells. PlGF binds only to VEGFR-1, which is also present on the surface of leucocytes. Activation of these receptors by VEGF-A can result in neovascularization and vascular permeability. Aflibercept is a dimeric glycoprotein which acts as a soluble decoy receptor that binds VEGF-A and PlGF, and thereby can inhibit the binding and activation of these cognate VEGF receptors.

POLICY

- Aflibercept for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Diabetic Macular Edema (DME)
  - Diabetic retinopathy (DR)
  - Neovascular age-related macular degeneration (AMD)
  - Macular edema following retinal vein occlusion (RVO)
- Aflibercept for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Aflibercept is considered **medically appropriate** if **ALL** of the following criteria are met:
  - Individual is 18 years of age or older
  - Individual is free from ocular and/or peri-ocular infections
  - Individual does not have active intraocular inflammation
  - Therapy will not be used with other ophthalmic VEGF inhibitors (i.e., brolucizumab-dbll, ranibizumab, pegaptanib, bevacizumab, etc.)
  - Individual has a definitive diagnosis of **ANY ONE** of the following:
    - Diabetic Macular Edema (DME)* and **ANY ONE** of the following (Initial Therapy only):
      - **BCBST requirement**: Individual must have an inadequate response to an adequate trial of bevacizumab OR bevacizumab-awwb OR bevacizumab-bvzr AND/OR ranibizumab prior to initiating treatment with aflibercept by meeting **ALL** of the following:
        - An adequate trial is defined as a minimum of 3 injections per affected eye of bevacizumab OR bevacizumab-awwb OR bevacizumab-bvzr AND/OR ranibizumab. The trial period must be completed within 168 days of initiation of therapy.
        - Inadequate response is defined as **ANY ONE** of the following:
          - After 3 injections of bevacizumab OR bevacizumab-awwb OR bevacizumab-bvzr AND/OR ranibizumab, Spectrum-Domain Optical Coherence Tomography (SD-OCT) central thickness reading of >350 µm OR visual acuity is equal to or worse than 20/50**

        - After 6 injections of bevacizumab OR bevacizumab-awwb OR bevacizumab-bvzr AND/OR ranibizumab, visual acuity is worse than 20/20 AND SD-OCT reading of >250 µm. The 6 injections must be completed within 1 year of initiation of therapy**
    - Treatment with aflibercept may be initiated if the individual has a documented contraindication or severe intolerance to BOTH Ranibizumab and **ANY ONE** of the following:
        - Bevacizumab
        - Bevacizumab-awwb
        - Bevacizumab-bvzr
- Diabetic retinopathy* and **ANY ONE** of the following (Initial Therapy only):
    - **BCBST requirement:** Individual must have an inadequate response to an adequate trial of bevacizumab OR bevacizumab-awwb OR bevacizumab-bvzr AND/OR ranibizumab prior to initiating treatment with aflibercept meeting **ALL** of the following:
        - An adequate trial is defined as a minimum of 3 injections per affected eye of bevacizumab OR bevacizumab-awwb OR bevacizumab-bvzr AND/OR ranibizumab. The trial period must be completed within 168 days of initiation of therapy.
        - Inadequate response is defined as **ANY ONE** of the following:
            - After 3 injections of bevacizumab OR bevacizumab-awwb OR bevacizumab-bvzr AND/OR ranibizumab, Spectrum-Domain Optical Coherence Tomography (SD-OCT) central thickness reading of >350 µm OR visual acuity is equal to or worse than 20/50**
            - After 6 injections of bevacizumab OR bevacizumab-awwb OR bevacizumab-bvzr AND/OR ranibizumab, visual acuity is worse than 20/20 AND SD-OCT reading of >250 µm. The 6 injections must be completed within 1 year of initiation of therapy**
    - Treatment with aflibercept may be initiated if the individual has a documented contraindication or severe intolerance to BOTH Ranibizumab and **ANY ONE** of the following:
        - Bevacizumab
        - Bevacizumab-awwb,
        - Bevacizumab-bvzr
- Neovascular (Wet) Age-Related Macular Degeneration (AMD)* and **BCBST requirement**: Documentation of prior trial and failure of **ANY ONE** of the following (Initial Therapy only):
    - Bevacizumab
    - Bevacizumab-awwb
    - Bevacizumab-bvzr
- Macular Edema following Retinal Vein Occlusion (RVO)

*Individuals with an insufficient response during initial therapy administered every 4 weeks may continue with dosing every 4 weeks. Individuals with an inadequate response to maintenance therapy administered every 8 weeks may increase the dosing frequency up to every 4 weeks. (Refer to Dosage and Administration)

**Optical Coherence Tomography (OCT) and VA testing must be completed within 56 days after the last injection of bevacizumab and/or ranibizumab when requesting aflibercept. We recommend physicians ensure patients have received a proper exam of their eyes by a qualified provider within the appropriate time frames to ensure individuals BCVA is optimal.

RENEWAL CRITERIA

- Aflibercept is considered **medically appropriate** for renewal if **ALL** of the following criteria are met:
    - Individual continues to meet initial approval criteria
    - Absence of unacceptable toxicity from the drug such as endophthalmitis and retinal detachments; increase in intraocular pressure; arterial thromboembolic events
    - Individual had a beneficial response to therapy

- Continued administration is necessary for the maintenance treatment of the condition

INDICATION(S)	DOSAGE & ADMINISTRATION
AMD	**Initiation:** 2 mg intravitreally per affected eye once every 4 weeks (approximately every 28 days, monthly) for the first 12 weeks (3 months) **Maintenance:** 2 mg intravitreally per affected eye once every 8 weeks (2 months); however 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 (approximately monthly) dosing after the first 12 weeks (3 months). • Patients may also be treated with one dose every 12 weeks after one year of effective therapy
Macular Edema following RVO	2 mg intravitreally per affected eye once every 4 weeks (approximately every 25 days, monthly)
Diabetic macular edema and diabetic retinopathy	**Initiation:** 2 mg intravitreally per affected eye once every 4 weeks (approximately every 28 days, monthly) for the first 5 injections **Maintenance:** 2 mg intravitreally per affected eye once every 8 weeks (2 months); however 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).

LENGTH OF AUTHORIZATION

Coverage will be provided annually and may be renewed.

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

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ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

Lexicomp Online. (2020, March). AHFS DI. *Aflibercept.* Retrieved October 5, 2020 from Lexicomp Online with AHFS.

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U. S. Food and Drug Administration. (2019, May). Center for Drug Evaluation and Research. *Eylea® (aflibercept) injection.* Retrieved October 5, 2020 from http://www.accessdata.fda.gov/drugsatfda_docs/label/2019/125387s052lbl.pdf.

Nguyen QD, Brown DM, Marcus DM, et al. Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE. *Ophthalmology* 2012; 119: 789–801. Retrieved December 5, 2017 doi.org/10.1016/j.ophtha.2011.12.039.

Wells JA, Glassman AR, Ayala AR, et al. Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema: Two-Year Results from a Comparative Effectiveness Randomized Clinical Trial. *Ophthalmology* 2016; 123 (6):1351-9. Retrieved December 5, 2017 doi.org/10.1016/j.ophtha.2016.02.022.

EFFECTIVE DATE 4/2/21

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