

PRIOR AUTHORIZATION POLICY

POLICY: Ophthalmology – Vascular Endothelial Growth Factor (VEGF) Inhibitor Injectables

- Eylea® (aflibercept intravitreal injection – Regeneron)
- Lucentis® (ranibizumab intravitreal injection – Genentech)
- Macugen® (pegaptanib sodium intravitreal injection – Valeant)

TAC APPROVAL DATE: 11/14/2018; Selected revision 5/20/2019

OVERVIEW

Intravitreal injection with vascular endothelial growth factor (VEGF) inhibitors is first-line therapy for neovascular (wet) age-related macular degeneration (AMD) and considered the treatment of choice for center-involving diabetic macular edema (DME).¹⁻² Commercially available intravitreal products include Eylea, Lucentis, and Macugen.³⁻⁵ Avastin® (bevacizumab intravenous [IV] infusion), indicated for use in certain cancerous conditions, is commonly compounded (as an intravitreal injection) and used off-label in wet AMD, DME, and other neovascular diseases of the eye.¹⁻² In addition to wet AMD, Eylea and Lucentis are indicated for the treatment of macular edema following retinal vein occlusion (RVO), DME, and diabetic retinopathy.³⁻⁴ Lucentis is also indicated for the treatment of myopic choroidal neovascularization (mCNV).⁴ However, because overproduction of VEGF may lead to other eye conditions, including neovascular glaucoma, retinopathy of prematurity, and other retinal and choroidal neovascular conditions affecting the eye,⁶ the VEGF inhibitors also have the potential to be used off-label and reduce vision loss associated with other eye conditions related to increased VEGF production.⁷ 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.⁸⁻⁹

Eylea, Lucentis, and Macugen differ in their pharmacology and pharmacokinetics.³⁻⁵ Lucentis is a monoclonal antibody fragment, Eylea is a fusion protein, and Macugen is an aptamer; however, all are designed to interfere with the activity of VEGF. Differences in molecular size, binding site, and binding affinity are some of the factors believed to affect the dosing schedule of the various products.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Eylea, Lucentis, and Macugen. Because of the specialized skills required for evaluation and diagnosis, the injection technique required, and the monitoring required for adverse events and long-term efficacy, approval requires the medication to be prescribed by or in consultation with an ophthalmologist. All approvals are provided for 1 year in duration unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

A. Coverage of Eylea is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **Neovascular (Wet) Age-Related Macular Degeneration (AMD).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Eylea is indicated for treatment of neovascular AMD.³

2. **Macular Edema Following Retinal Vein Occlusion (RVO).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Eylea is indicated for treatment of macular edema following RVO.³

3. **Diabetic Macular Edema (DME).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Eylea is indicated for treatment of DME.³

4. **Diabetic Retinopathy.** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Eylea is indicated for treatment of diabetic retinopathy.³

Other Uses with Supportive Evidence

5. **Other Neovascular Diseases of the Eye (e.g., neovascular glaucoma, retinopathy of prematurity, sickle cell neovascularization, choroidal neovascular conditions, etc.).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

VEGF has a role in ocular angiogenesis for conditions such as diabetic retinopathy, macular edema, and RVO.⁹⁻¹⁰ VEGF inhibitors may stop the angiogenic process, thus maintaining and/or improving vision. Multiple other causes of retinal and choroidal neovascularization exist. Anti-VEGF therapy has the potential to be used off-label in other neovascular conditions affecting the eye and may prevent or slow visual impairment.⁷⁻⁹

- B. Coverage of Lucentis is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **Neovascular (Wet) Age-Related Macular Degeneration (AMD).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Lucentis is indicated for treatment of neovascular AMD.⁴

2. **Macular Edema Following Retinal Vein Occlusion (RVO).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Lucentis is indicated for treatment of macular edema following RVO.⁴

3. **Diabetic Macular Edema (DME).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Lucentis is indicated for treatment of DME.⁴

- 4. Diabetic Retinopathy.** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Lucentis is indicated for treatment of diabetic retinopathy.⁴

- 5. Myopic Choroidal Neovascularization (mCNV).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Lucentis is indicated for treatment of mCNV.⁴

Other Uses with Supportive Evidence

- 6. Other Neovascular Diseases of the Eye (e.g., neovascular glaucoma, retinopathy of prematurity, sickle cell neovascularization, choroidal neovascular conditions, etc.).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

VEGF has a role in ocular angiogenesis for conditions such as diabetic retinopathy, macular edema, and RVO.⁹⁻¹⁰ VEGF inhibitors may stop the angiogenic process, thus maintaining and/or improving vision. Multiple other causes of retinal and choroidal neovascularization exist. Anti-VEGF therapy has the potential to be used off-label in other neovascular conditions affecting the eye and may prevent or slow visual impairment.⁷⁻⁹

- C. Coverage of Macugen is recommended in those who meet the following criteria:

FDA-Approved Indications

- 1. Neovascular (Wet) Age-Related Macular Degeneration (AMD).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Macugen is indicated for treatment of neovascular (wet) AMD.⁵

Other Uses with Supportive Evidence

- 2. Other Neovascular Diseases of the Eye (e.g., diabetic retinopathy, neovascular glaucoma, retinopathy of prematurity, sickle cell neovascularization, choroidal neovascular conditions, etc.).** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

VEGF has a role in ocular angiogenesis for conditions such as diabetic retinopathy, macular edema, and RVO.⁹⁻¹⁰ VEGF inhibitors may stop the angiogenic process, thus maintaining and/or improving vision. Multiple other causes of retinal and choroidal neovascularization exist. Anti-VEGF therapy has the potential to be used off-label in other neovascular conditions affecting the eye and may prevent or slow visual impairment.⁷⁻⁹

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Eylea, Lucentis, and Macugen have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-related macular degeneration. San Francisco, CA: American Academy of Ophthalmology; 2015. Accessed on October 29, 2018. Available at: www.aao.org/ppp
2. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic retinopathy. San Francisco, CA: American Academy of Ophthalmology; 2017. Accessed on October 29, 2018. Available at: www.aao.org/ppp
3. Eylea® injection [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; May 2019.
4. Lucentis® intravitreal injection [prescribing information]. South San Francisco, CA: Genentech, Inc.; April 2017.
5. Macugen® injection [prescribing information]. Cedar Knolls, NJ: Eyetech Inc.; October 2011.
6. Tolentino M. Systemic and ocular safety of intravitreal anti-VEGF therapies for ocular neovascular disease. *Surv Ophthalmol*. 2011;56(2):95-113.
7. Barakat MR, Kaiser PK. VEGF inhibitors for the treatment of neovascular age-related macular degeneration. *Expert Opin Investig Drugs*. 2009;18(5):637-646.
8. Kinnunen K, Ylä-Herttua S. Vascular endothelial growth factors in retinal and choroidal neovascular diseases. *Ann Med*. 2012;44(1):1-17.
9. Horsley MB, Kahook MY. Anti-VEGF therapy for glaucoma. *Curr Opin Ophthalmol*. 2010;21(2):112-117.
10. Ip MS, Scott IU, Brown GC, et al. Anti-vascular endothelial growth factor pharmacotherapy for age-related macular degeneration: a report by the American Academy of Ophthalmology. *Ophthalmology*. 2008;115(10):1837-1846.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No change to criteria.	11/16/2016
Selected revision	Added new FDA-approved indication for Lucentis for mCNV.	01/18/2017
Selected revision	Revised indication for Lucentis for diabetic retinopathy.	05/17/2017
Annual revision	No change to criteria.	11/29/2017
Annual revision	Updated duration of approvals to 1 year.	11/14/2018
Selected revision	For Eylea, the condition, Diabetic retinopathy in patients with Diabetic Macular Edema, was update to include all patients with Diabetic Retinopathy. Previously the product was only indicated to treatment Diabetic Retinopathy in patients who also had DME.	05/23/2019

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; DME – Diabetic macular edema; RVO – Retinal vein occlusion; mCNV – Myopic choroidal neovascularization.