MEDICAL MUTUAL®

MedicalPolicy

Policy:	**201513**	**Initial Effective Date: 04/30/2015**
Code(s):	**HCPCS J0178, J2503 and J2778**	**Annual Review Date: 03/15/2018**
SUBJECT:	**Ophthalmic Vascular Endothelial Growth Factor (VEGF) Inhibitor Injectable Drugs for Macular Degeneration** • **Eylea® (aflibercept intravitreal injection),** • **Lucentis® (ranibizumab intravitreal injection),** • **Macugen® (pegaptanib sodium intravitreal injection)**	**Last Revised Date: 09/20/2018**

Prior approval is required for some or all procedure codes listed in this Corporate Medical Policy.

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 also indicated for the treatment of macular edema following retinal vein occlusion (RVO); DME; and diabetic retinopathy in patients with DME.[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 required for 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 for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

Recommended Authorization Criteria
Coverage of Eylea, Lucentis, and Macugen is recommended in those who meet one of the following criteria:

Food and Drug Administration (FDA)-Approved Indications

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

1. **Neovascular (Wet) Age-Related Macular Degeneration (AMD).[2] Approve** if administered by or under the supervision of an ophthalmologist.

Dosing in Neovascular (Wet) Age-Related Macular Degeneration (AMD). *FDA approved label recommends*:
2 mg intravitreal injection for each eye treated every 4 weeks (monthly) for the first 12 weeks (3 months) followed by
2 mg intravitreal injection for each eye treated once every 8 weeks (2 months). Patients with persistent retinal fluid visible via Optical Coherence Tomography (OCT) after the initial 3 months can qualify for every 4 week (monthly) continuation dosing. Some patients are eligible for dosing once every 12 weeks after they have been treated successfully for at least one year.

Initial Approval/Extended Approval for Neovascular (Wet) Age-Related Macular Degeneration (AMD).
a) *Initial Approval:* Initial approval is for 3 months of therapy.
b) *Extended Approval:* Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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

Dosing in Macular Edema Following Retinal Vein Occlusion (RVO). *FDA approved label recommends:* 2 mg intravitreal injection for each eye treated once every 4 weeks (monthly).

Initial Approval/Extended Approval for RVO:
a) *Initial Approval:* Initial approval is for 12 months of therapy.
b) *Extended Approval:* Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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3. **Diabetic Macular Edema (DME).**[2] Approve if administered by or under the supervision of an ophthalmologist.

Dosing in Diabetic Macular Edema (DME). *FDA approved label recommends:*
2 mg intravitreal injection for each eye treated every 4 weeks (monthly) for the first 5 injections.
After 5 months, approve cases requesting 2 mg every 8 weeks. Those cases requesting 2 mg every 4 week dosing should be reviewed by a physician as some patients may require every 4 week (monthly) dosing. Some patient may need every 4 week dosing after the first 20 weeks.

Initial Approval/Extended Approval for DME:
a) *Initial Approval:* Initial approval is for 5 months of therapy.
b) *Extended Approval:* Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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4. **Diabetic Retinopathy in Patients with Diabetic Macular Edema (DME).**[2] Approve if administered by or under the supervision of an ophthalmologist.

Dosing in Diabetic Retinopathy in Patients with Diabetic Macular Edema (DME). *FDA approved label recommends:*
2 mg intravitreal injection for each eye treated every 4 weeks (monthly) for the first 5 injections. After 5 months, approve cases requesting 2 mg every 8 weeks. Those cases requesting 2 mg every 4 week dosing should be reviewed by a physician as some patients may require every 4 week (monthly) dosing. Some patient may need every 4 week dosing after the first 20 weeks.

Initial Approval/Extended Approval for DME and DR
a) *Initial Approval:* Initial approval is for 5 months of therapy.
b) *Extended Approval:* Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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 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. 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

Initial Approval/Extended Approval for Other Neovascular Diseases of the Eye.
a) *Initial Approval:* Initial approval is for 12 months of therapy.
b) *Extended Approval:* Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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

1. **Neovascular (Wet) Age-Related Macular Degeneration (AMD).**[3] Approve if administered by or under the supervision of an ophthalmologist.

Dosing in Neovascular (Wet) Age-Related Macular Degeneration (AMD). *FDA approved label recommends:* 0.5 mg intravitreal injection for each eye treated once monthly (approximately 28 days).

Initial Approval/Extended Approval.
a) *Initial Approval:* Initial approval is for 12 months of therapy.
b) *Extended Approval*: Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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2. **Macular Edema Following Retinal Vein Occlusion (RVO).**[3] Approve if administered by or under the supervision of an ophthalmologist.

Dosing in Macular Edema Following Retinal Vein Occlusion (RVO). *FDA approved label recommends:* 0.5 mg intravitreal injection for each eye treated once monthly (approximately 28 days).

Initial Approval/Extended Approval.
a) *Initial Approval:* Initial approval is for 12 months of therapy.
b) *Extended Approval*: Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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

Dosing in Diabetic Macular Edema (DME). *FDA approved label recommends:* 0.3 mg intravitreal injection for each eye treated once monthly (approximately 28 days).

Initial Approval/Extended Approval.
a) *Initial Approval:* Initial approval is for 12 months of therapy.
b) *Extended Approval*: Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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4. **Diabetic Retinopathy in Patients with or without Diabetic Macular Edema (DME).**[3] Approve if administered by or under the supervision of an ophthalmologist.

Dosing in Diabetic Retinopathy in Patients with or without Diabetic Macular Edema (DME). *FDA approved label recommends:* 0.3 mg intravitreal injection for each eye treated once monthly (approximately 28 days).

Initial Approval/Extended Approval.
a) *Initial Approval:* Initial approval is for 12 months of therapy.
b) *Extended Approval*: Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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5. Myopic Choroidal Neovascularization (mCNV). Approve if administered by or under the supervision of an ophthalmologist.

Dosing in mCNV. *FDA approved label recommends:* Intravitreal: 0.5 mg once a month (approximately every 28 days) for up to 3 months; may retreat if necessary.

Initial Approval/Extended Approval.
a) *Initial Approval:* Initial approval is for 12 months of therapy.

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b) *Extended Approval*: Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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6. **Other Neovascular Diseases of the Eye (e.g., neovascular glaucoma, retinopathy of prematurity, sickle cell neovascularization, choroidal neovascular conditions, etc.).** Approve 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. 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.

Initial Approval/Extended Approval.
a*) Initial Approval:* Initial approval is for 12 months of therapy.
b) *Extended Approval*: Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

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

1. **Neovascular (Wet) Age-Related Macular Degeneration (AMD).**[4] Approve if administered by or under the supervision of an ophthalmologist.

Dosing in Neovascular (Wet) Age-Related Macular Degeneration (AMD). *FDA approved label recommends:* 0.3 mg intravitreal injection for each eye treated every six weeks.

Initial Approval/Extended Approval.
a) *Initial Approval:* Initial approval is for 12 months of therapy.
b) *Extended Approval:* Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

Other Uses with Supportive Evidence

2. **Other Neovascular Diseases of the Eye (e.g., neovascular glaucoma, retinopathy of prematurity, sickle cell neovascularization, choroidal neovascular conditions, etc.).** Approve 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. 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.

Initial Approval/Extended Approval.

a) *Initial Approval:* Initial approval is for 12 months of therapy.

b) *Extended Approval:* Approve at additional 12-month intervals if the patient has a response or has maintained response with no further progression of disease, as determined by the prescribing physician.

D. Patient has been Established on Eylea, Lucentis, and Macugen. Approve for 12 months if the patient meets the conditions for coverage required for **Dosing**, **and Extended Approval** for an approved use in this *Ophthalmic Vascular Endothelial Growth Factor (VEGF) Inhibitor Injectable Drugs for Macular Degeneration Utilization Review* policy.

Exclusions.

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. Rationale for non-coverage for these specific conditions is provided below. (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.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive.
Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

Prior approval is required for HCPCS Codes J0178, J2503 and J2778

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 November 24, 2017. 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; 2016. Accessed on November 24, 2017. Available at: www.aao.org/ppp
3. Eylea® injection [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; May 2017.
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-Herttuala 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.

HCPCS Code(s):	
J0178	Injection, aflibercept, 1 mg
J2503	Injection, pegaptanib sodium, 0.3 mg
J2778	Injection, ranibizumab, 0.1 mg