Medicare Advantage Medical Utilization Review Policy

Policy:	**Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Ranibizumab Products Utilization Management Medical Policy** • Byooviz™ (ranibizumab-nuna intravitreal injection – Biogen) • Cimerli™ (ranibizumab-eqrn intravitreal injection – Coherus) • Lucentis® (ranibizumab intravitreal injection – Genentech)
Date:	12/11/2023
Applicable Lines of Business:	Medicare Advantage - Medical
Applicable States:	NGS, J6: Wisconsin, Minnesota, Illinois NGS, JK: New York, Connecticut, Massachusetts, Maine, New Hampshire, Rhode Island, Vermont

OVERVIEW

Lucentis and Cimerli (interchangeable biosimilar to Lucentis) are vascular endothelial growth factor (VEGF) inhibitors indicated for the following uses:[1,7]

- **Diabetic macular edema**.
- **Diabetic retinopathy**.
- **Macular edema following retinal vein occlusion**.
- **Myopic choroidal neovascularization**.
- **Neovascular (wet) age-related macular degeneration**.

Byooviz (interchangeable biosimilar to Lucentis) is indicated for the following uses:[6]

- **Macular edema following retinal vein occlusion**.
- **Myopic choroidal neovascularization**.
- **Neovascular (wet) age-related macular degeneration**.

The recommended dosing for each of the indication is as follows:[1,6,7]

- **Diabetic macular edema, diabetic retinopathy:** 0.3 mg administered by intravitreal injection once every month (approximately 28 days) [Cimerli and Lucentis]
- **Macular edema following retinal vein occlusion, neovascular (wet) age-related macular degeneration:** 0.5 mg administered by intravitreal injection once every month (approximately 28 days).
- **Myopic choroidal neovascularization:** 0.5 mg administered by intravitreal injection once every month (approximately 28 days) for up to 3 months; patients may be retreated if needed.

Other Uses with Supportive Evidence

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.[2,3] The VEGF inhibitors have the potential to be used off-label to reduce or slow visual impairment or vision loss associated with other eye conditions related to increased VEGF production.[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.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of ranibizumab products. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). All approvals are provided for the duration noted below.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of ranibizumab products is recommended in those who meet the following criteria.

FDA-Approved Indications

1. Neovascular (Wet) Age-Related Macular Degeneration.

Criteria. Approve for 1 year.

Dosing. Approve if the requested dosing meets the following (A and B):
A) The dose is 0.5 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 28 days for each eye being treated.

2. Macular Edema Following Retinal Vein Occlusion.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both criteria (A and B):
A) The dose is 0.5 mg administered by intravitreal injection for each eye being treated; AND

B) The dosing interval is not more frequent than once every 28 days for each eye being treated.

---

3. Diabetic Macular Edema.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both criteria (A and B):
A) The dose is 0.3 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 28 days for each eye being treated.

---

4. Diabetic Retinopathy.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both criteria (A and B):
A) The dose is 0.3 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 28 days for each eye being treated.

---

5. Myopic Choroidal Neovascularization.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both criteria (A and B):
A) The dose is 0.5 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 28 days for each eye being treated.

Other Uses with Supportive Evidence

---

6. Other Neovascular Diseases of the Eye.
Note: Examples of other neovascular diseases of the eye include neovascular glaucoma, retinopathy of prematurity, sickle cell neovascularization, choroidal neovascular conditions.

Criteria. Approve for 1 year.

Dosing. Approve if the dose meets both criteria (A and B):
A) The dose is 0.5 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 28 days for each eye being treated.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Coverage of ranibizumab productsis not recommended in the following situations:

---

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. Lucentis® intravitreal injection [prescribing information]. South San Francisco, CA: Genentech; August 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. Byooviz™ intravitreal injection [prescribing information]. Cambridge, MA: Biogen; October 2023.
7. Cimerli™ intravitreal injection [prescribing information]. Redwood City, CA: Coherus; August 2022.
8. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Determination (LCD): Drugs and Biologicals, Coverage of, for Label and Off-Label Uses (L33394) [original date 10/01/2015; revision effective date 11/1/2022]. Accessed on December 11, 2023.
9. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Article (LCA): Billing and Coding: Ranibizumab, Aflibercept and Brolucizumab-dbll (A52451) [original date 10/01/2015; revision effective date 04/21/2023]. Accessed on December 11, 2023.

HISTORY

Type of Revision	Summary of Changes*	Date
Policy created	New Medicare Advantage Medical Policy	07/11/2018
Select revision	Added Macugen to policy	11/05/2018
Select revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52451 and Ophthalmology – Vascular Endothelial Growth Factor (VEGF) Inhibitor Injectables Utilization Review Policy.	5/22/2019
Select revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Determination L33394 and Ophthalmology – Vascular Endothelial Growth Factor Inhibitors - Lucentis Utilization Review Policy.	11/06/2019
Select revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020
Policy revision	*Added the following to the Policy Statement "Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy	08/07/2020

	may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles." *Updated references	
Policy revision	**Macular Edema Following Retinal Vein Occlusion, Myopic Choroidal Neovascularization,** and **Neovascular (Wet) Age-Related Macular Degeneration:** To align with the FDA-approved dosing, the dose was changed from "≤ 0.5 mg" to "is 0.5 mg". **Diabetic Macular Edema** and **Diabetic Retinopathy:** To align with the FDA-approved dosing, the dose was changed from "≤ 0.3 mg" to "is 0.3 mg". **Other Neovascular Ophthalmic Conditions:** Examples of other neovascular diseases of the eye were moved to a Note. To align with the FDA-approved dosing, the dose was changed from "≤ 0.5 mg" to "is 0.5 mg".	12/20/2021
Policy revision	**Title:** The name was changed by replacing "Lucentis" with "Ranibizumab Products". Now reads, Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Ranibizumab Products Utilization Management Medical Policy. **Product:** Byooviz was added to the same conditions for approval as for Lucentis.	06/29/2022
Policy revision	**Product:** Cimerli was added to the same conditions for approval as for the other ranibizumab products.	09/29/2022
Policy revision	For all indications/uses, the dosing interval was changed from "not more frequent than once every 25 days for each eye being treated" to "not more frequent than once every 28 days for each eye being treated"; the 28 days aligns with the prescribing information.	12/11/2023