Effective Date **4/1/2023**
Next Review Date… **4/1/2024**
Coverage Policy Number **IP0543**

Ranibizumab

Table of Contents

Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following Ranibizumab Products:

- Byooviz™ (ranibizumab-nuna) intravitreal injection
- Cimerli™ (ranibizumab-eqrn) intravitreal injection
- Lucentis® (ranibizumab) intravitreal injection

Coverage for Ranibizumab Products (Byooviz, Cimerli, and Lucentis) varies across plans and requires the use of preferred products in addition to the criteria listed below. Refer to the customer's benefit plan document for coverage details.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Initial Approval Criteria

Ranibizumab for intravitreal injection (Lucentis), ranibizumab-eqrn for intravitreal injection (Cimerli) and ranibizumab-nuna for intravitreal injection (Byooviz) are considered medically necessary when the individual meets ALL of the following criteria:

1. Treatment of **ONE** of the following
    a. Diabetic Macular Edema (DME)
    b. Diabetic Retinopathy (DR)
    c. Macular Edema following retinal vein occlusion (RVO)
    d. Myopic Choroidal Neovascularization (mCNV)
    e. Neovascular (wet) Age-Related Macular Degeneration (AMD)
    f. Ocular Histoplasmosis Syndrome
    g. Other Neovascular Diseases of the Eye (for example, neovascular glaucoma, retinopathy of prematurity, sickle cell neovascularization, choroidal neovascular conditions)
2. Medication is administered by, or under the supervision of, an ophthalmologist
3. Preferred products are required, refer to below table:

Employer Group and Individual and Family Plan Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Byooviz (ranibizumab-nuna) for intravitreal injection	**ONE** of the following: 1. Currently receiving Byooviz 2. **ONE** of the following: a. Documentation of failure, contraindication, or intolerance to repackaged bevacizumab b. If, in the professional opinion of the prescriber, the safety of using the repackaged bevacizumab or the supplier of the repackaged bevacizumab is of significant concern 3. Diabetic retinopathy
Cimerli (ranibizumab-eqrn) for intravitreal injection	**ONE** of the following: 1. Currently receiving Cimerli 2. **ONE** of the following: a. Documentation of failure, contraindication, or intolerance to repackaged bevacizumab b. If, in the professional opinion of the prescriber, the safety of using the repackaged bevacizumab or the supplier of the repackaged bevacizumab is of significant concern **3.** Diabetic retinopathy
Lucentis (ranibizumab) for intravitreal injection	**ONE** of the following: 1. Currently receiving Lucentis 2. **ONE** of the following: a. Documentation of failure, contraindication, or intolerance to repackaged bevacizumab b. If, in the professional opinion of the prescriber, the safety of using the repackaged bevacizumab or the supplier of the repackaged bevacizumab is of significant concern **3.** Diabetic retinopathy

Dosing. The recommended dose of Ranibizumab Products (Byooviz, Cimerli, Lucentis) for Diabetic Macular Edema and Diabetic Retinopathy, is:

1. 0.3 mg administered by intravitreal injection for each eye being treated
2. The dosing interval is not more frequent than once every 25 days for each eye being treated

Dosing. The recommended dose of Ranibizumab Products (Byooviz, Cimerli, Lucentis) for Macular Edema Following Retinal Vein Occlusion, Myopic Choroidal Neovascularization, Neovascular (Wet) Age-Related Macular Degeneration, Ocular Histoplasmosis and Other Neovascular Diseases of the Eye (for example, neovascular glaucoma, retinopathy of prematurity, sickle cell neovascularization, choroidal neovascular conditions), is:

1. 0.5 mg administered by intravitreal injection for each eye being treated
2. The dosing interval is not more frequent than once every 25 days for each eye being treated

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Continuation of Therapy

Continuation of Ranibizumab Products (Byooviz, Cimerli, Lucentis) is considered medically necessary for ALL Covered Diagnoses when initial criteria are met AND beneficial response is demonstrated.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J2778	Injection, ranibizumab, 0.1 mg
Q5124	Injection, ranibizumab-nuna, biosimilar, (Byooviz), 0.1 mg
Q5128	Injection, ranibizumab-eqrn (cimerli), biosimilar, 0.1 mg (Code effective 04/01/2023)

Background

OVERVIEW
Lucentis and Cimerli (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 (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 dose for Lucentis and Cimerli in diabetic macular edema and diabetic retinopathy is 0.3 mg administered by intravitreal injection once every month (approximately 28 days). The recommended dose for Byooviz, Cimerli, and Lucentis in neovascular (wet) age-related macular degeneration, macular edema following retinal vein occlusion, and myopic choroidal neovascularization is 0.5 mg administered by intravitreal injection once every month (approximately 28 days).
Byooviz is available in a single-use vial designed to provide 0.05 mL of 10 mg/mL solution for intravitreal injection.
Cimerli is available in single-dose glass vials designed to provide 0.05 mL for intravitreal injection 10 mg/mL solution (0.5 mg) and 6 mg/mL solution (0.3 mg).
Lucentis is available in single-use, 2-mL glass vial designed to provide 0.05 mL for intravitreal injection 6 mg/mL solution and 10 mg/mL solution. Single-use prefilled syringe designed to provide 0.05 mL for intravitreal injections 10 mg/mL solution.

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 also have the potential to be used off-label and reduce vision loss associated with other eye conditions related to increased VEGF production. 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.[4,5] 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.[2,4,5]

Additional Clinical Information
The effect of ranibizumab on choroidal neovascularization, secondary to causes other than age-related macular degeneration, was studied in a randomized, controlled trial, and included 9 patients with ocular histoplasmosis syndrome. Thirty patients were randomized to either monthly intravitreal ranibizumab or 3 monthly intravitreal injections followed by PRN injections of ranibizumab. Results revealed no difference between the groups in visual acuity or central retinal thickness. In addition, a retrospective chart review of 52 patients treated with either bevacizumab or ranibizumab showed significant improvement in visual acuity from baseline in patients with choroidal neovascularization secondary to OHS.[8]

References

1. Lucentis® intravitreal injection [prescribing information]. South San Francisco, CA: Genentech; October 2020.
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; September 2022.
7. Cimerli™ intravitreal injection [prescribing information]. Redwood City, CA: Coherus; October 2022.

Supplemental References

8. Heier JS et al. Ranibizumab for choroidal neovascularization secondary to causes other than age-related macular degeneration: a phase 1 clinical trial. Ophthalmology 2011; 118: 111-8.