Reference number(s)
2508-A

Standard Medicare Part B Management
Lucentis - Byooviz -Cimerli

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) OTC products are not included unless otherwise stated.

Brand Name	Generic Name
Lucentis	ranibizumab
Byooviz	ranibizumab-nuna
Cimerli	ranibizumab-eqrn

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1,3,4]

Lucentis, Byooviz and Cimerli are indicated for:

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

Lucentis and Cimerli are also indicated for:

- Diabetic macular edema
- Diabetic retinopathy

Compendial Uses[2]

Retinopathy of prematurity

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

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Coverage Criteria

Neovascular (wet) age-related macular degeneration[1,3,4]

Authorization of 12 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

Macular edema following retinal vein occlusion[1,3,4]

Authorization of 12 months may be granted for treatment of macular edema following retinal vein occlusion.

Diabetic macular edema[1,4]

Authorization of 12 months may be granted for the treatment of diabetic macular edema.

Diabetic retinopathy[1,4]

Authorization of 12 months may be granted for the treatment of diabetic retinopathy.

Myopic choroidal neovascularization[1,3,4]

Authorization of 12 months may be granted for the treatment of myopic choroidal neovascularization.

Retinopathy of prematurity[2]

Authorization of 12 months may be granted for the treatment of retinopathy of prematurity.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization of 12 months may be granted when ALL of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat an indication in the coverage criteria section.
- The member demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or vision field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Lucentis, Byooviz, and Cimerli
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Lucentis, Byooviz and Cimerli are covered in addition to retinopathy of prematurity.

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for retinopathy of prematurity can be found in a retrospective single center study of 128 infants with Type 1 ROP and 18-month follow-up examinations found recurrence rates of 16.7% (1 of 6 patients) with intravitreal ranibizumab 0.25 mg and 8.3% (1 of 12 patients) with intravitreal bevacizumab 0.625 mg following initial regression within 48 hours in all patients who received either ranibizumab or bevacizumab. Recurrence was defined as recurrent plus or preplus disease or neovascularization, or progression of traction. In a third group of 36 patients who received LPC therapy, initial regression occurred in 1 to 2 weeks except in 5 patients who required retreatment with LPC at 10 days. Differences in the ranibizumab, bevacizumab, and LPC groups at baseline were found in birth weight (840, 841, and 1112 grams, respectively), number of patients with Stage 3 disease (16.7%, 16.7%, and 61.1%, respectively), APROP (83.3%, 83.3%, and 19.4%, respectively), and Zone II disease (66.7%, 83.3%, and 88.9%, respectively). A fourth group of 74 patients with spontaneously regressed ROP was included. The two patients who recurred after ranibizumab or bevacizumab therapy achieved successful regression following subsequent LPC therapy. Mean total vascularization time was significantly shorter with ranibizumab (61.8 weeks of PMA) compared with bevacizumab (73 weeks of PMA). Following LPC, one patient experienced exudative retinal detachment and nystagmus in both eyes and one patient had macular ectopia and nystagmus; no ocular complications were noted in other groups other than transient preretinal hemorrhages.

Ranibizumab compared with laser photocoagulation (LPC), did not demonstrate a significant difference for the primary outcome (composite of survival with no active retinopathy, no unfavorable structural outcomes, or need for a different treatment modality at 24 weeks; 80% vs 66%; OR, 2.19; 95% CI, 0.99 to 4.82) in the randomized RAINBOW trial in infants with retinopathy of prematurity (ROP; N=214). Included infants (median gestational age 26 weeks) had bilateral ROP zone I stage 1+, 2+, 3, or 3+, zone II stage 3+, or aggressive posterior ROP (AP-ROP). Infants with zone II stage 2+ were excluded. Treatment success (alive and without treatment switch and unfavorable structural outcome or active ROP at day 169) was not significantly different between groups; achieved in 80% with ranibizumab 0.2 mg, 75% with ranibizumab 0.1 mg, and 66% with laser therapy. In a post-hoc analysis accounting for potential confounders (gestational age, geographical region, and gender) the primary outcome was significant for ranibizumab 0.2 mg compared with laser (OR 2.32; 95% CI, 1.04 to 5.16). There was no significant between-group difference in the plasma vascular endothelial growth factor (VEGF) levels. There was 1 death associated with ranibizumab 0.1 mg or the procedure due to respiratory failure. Interventions included a single bilateral intravitreal dose of ranibizumab 0·2 mg, 0·1 mg, or laser therapy. The ranibizumab groups were permitted up to 2 additional treatments in each eye at a minimum of

28-day intervals and in the laser group supplementary treatment to skip lesions was allowed up to day 11. Additional treatments were needed in 31% with ranibizumab 0.2 mg , 31% with ranibizumab 0.1 mg, and 19% with laser therapy.

References

1. Lucentis [package insert]. South San Francisco, CA: Genentech, Inc.; February 2024.
2. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com/. Accessed February 15, 2024.
3. Byooviz [package insert]. Cambridge, MA: Biogen, Inc.; October 2023.
4. Cimerli [package insert]. Redwood City, CA: Coherus BioSciences, Inc.; November 2022.
5. Kabatas EU, Kurtul BE, Altiaylik Ozer P, et al: Comparison of intravitreal bevacizumab, intravitreal ranibizumab and laser photocoagulation for treatment of type 1 retinopathy of prematurity in Turkish preterm children. Curr Eye Res 2017; 42(7):1054-1058.
6. Stahl A , Lepore D , Fielder A , et al: Ranibizumab versus laser therapy for the treatment of very low birthweight infants with retinopathy of prematurity (RAINBOW): an open-label randomised controlled trial. Lancet 2019; 394(10208):1551-1559.