This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the IEHP Pharmacy and Therapeutic Subcommittee.

**Drug:** Lucentis (ranibizumab)  
**Class:** Vascular endothelial growth factor (VEGF) inhibitor  
**Effective Date:** November 19, 2014  
**Revision Date:** November 19, 2014

**Policy/Criteria:**

**Use of Lucentis:**

1. Treatment of neovascular “wet” age related macular degeneration  
   a. Must be prescribed by ophthalmologist

2. Treatment of macular edema following retinal vein occlusion  
   a. Must be prescribed by ophthalmologist

3. Treatment of diabetic macular edema  
   a. Must be prescribed by ophthalmologist

**Other Alternative - Use of Avastin will also be allowed per criteria below:**

1. Treatment of neovascular “wet” age-related macular degeneration  
   a. Confirmed diagnosis of neovascular “wet” age-related macular degeneration  
   b. Must be prescribed by ophthalmologist  
   c. If patient is likely to have a therapeutic response with the use of intravitreal bevacizumab, may be used in lieu of Lucentis

Note: J3490 with explanation of procedure and dosage used should be submitted for billing purposes.

**Clinical Justification:**

Age Related Macular Degeneration

1. Avastin (bevacizumab) is a recombinant humanized monoclonal IgG1 antibody that is similar to Lucentis.
2. American Academy of Ophthalmology supported the reimbursement for treating age-related macular degeneration (AMD) with intravitreal injections of bevacizumab, to meet the medical needs of many patients who have not responded to therapy with ocular photodynamic therapy (OPT) with verteporfin or intravitreal pegaptanib.

3. More than 6,800 injections in 5,055 patients from 68 centers in 12 countries have been documented with a low rate of ocular or systemic adverse events.

4. The use of Avastin via intravitreal injection is entirely off-label, but the clinical experiences appear that Avastin works as well as Lucentis.

5. Avastin is formulated for intravenous infusion, not intravitreal injection. Although Avastin is similar to Lucentis, they are different in several aspects:
   a. Avastin is about 3 times as large as Lucentis (149kD vs. 48kD) - smaller molecular means better penetration to the layers of the retina;
   b. Avastin has a longer half-life (20 days compared to 4 hours)- less systemic side-effects if it is significant;
   c. Lucentis does not have the Fc portion of the antibody fragment, which may cause less inflammation within the eye.

Macular Edema associated with Retinal Vein Occlusion

1. Ranibizumab, a VEGF-inhibitor, is approved by FDA for the treatment of macular edema due to retinal vein occlusion

2. Laser photocoagulation is an established therapy for retinal vein occlusion. Although there is limited data directly comparing laser therapy and VEGF-inhibitors, visual benefit may be noted earlier with VEGF-inhibitor therapy than those treated with laser therapy.

3. Ranibizumab intravitreal therapy significantly improved visual acuity in comparison to sham (placebo) injections in two randomized, double blind studies that involved patients with macular edema due to central or branch retinal vein occlusion.

Diabetic Macular Edema

1. Ranibizumab, a VEGF-inhibitor, is approved by FDA for the treatment of diabetic macular edema.

2. Phase III trials resulted in significant improvement in visual acuity and anatomic outcomes in the study group of ranibizumab in comparison to the control. Furthermore, ranibizumab as monotherapy as well as in conjunction with laser therapy associated with superior visual benefits than laser therapy alone.

3. However, the long-term safety and efficacy data is not yet well established beyond two years.

Precautions and Adverse Effects

1. Serious adverse ocular events include endophthalmitis, retinal detachment and traumatic cataract with less than 0.1% incidence. Other adverse effects include vitreous and conjunctival hemorrhage, eye pain and intraocular pressure elevation.

2. Ranibizumab is not recommended for patients with active bacterial ocular or periocular infection.
3. According to Antiplatelet Trialists’ Collaboration (APTC) criteria, cerebrovascular accidents or other vascular or unknown cause associated mortality is slightly higher in the study group (ranibizumab) in the RISE and RIDE trials. However, the trend of systemic vascular adverse events has not been observed consistently among all other trials. Further study will be required to confirm the systemic vascular adverse effect of ranibizumab.

REFERENCES:

11. Rosenfeld PJ. Intravitreal bevacizumab for CNV and DME. Program and abstracts of the Association for Research in Vision and Ophthalmology; April 30-May 4, 2006; Fort Lauderdale, Florida. Significant Interest Group 251.