Subject: Macugen® (pegaptanib)

Overview: Macugen is an injectable drug used to treat select eye conditions.

Policy and Coverage Criteria:

NOTE: Prior Authorization is not required

Harvard Pilgrim considers the use of Macugen medically necessary for the treatment of any of the following:
- Neovascular age-related macular degeneration (AMD); or
- Diabetic Macular Edema (DME); or
- Diabetic Retinopathy.

Harvard Pilgrim does not cover the use of Macugen for conditions or diagnoses other than those listed above.

Exclusions: N/A

Supporting Information:
1. Technology Assessment: Macugen (pegaptanib) is a pegylated synthetic aptamer designed to inhibit VEGF, inhibiting the abnormal blood vessel growth associated with neovascular age-related macular degeneration.
2. Literature Review:
Sultan et al (2011) conducted a randomized, sham-controlled, parallel-group trial to confirm the safety and compare the efficacy of intravitreal pegaptanib sodium 0.3 mg versus sham injections in 467 patients with DME involving the center of the macula associated with vision loss not due to ischemia. Patients received 0.3 mg of pegaptanib or sham injections every 6 weeks for 1 year and could receive focal/grid coagulation beginning at week 18. Patients received injections as often as every 6 weeks during week 2. 36.8% of patients from the pegaptanib group and 19.7% from the sham group experienced a visual acuity improvement of ≥ 10 letters at week 54 compared with baseline. For pegaptanib-treated patients, change in mean visual acuity from baseline by visit was significantly superior to sham at weeks 6, 24, 30, 36, 42, 54, 78, 84, 90, 96, and 102. At week 102, pegaptanib-treated patients gained, on average, 6.1 letters versus 1.3 letters for sham. Fewer pegaptanib- than sham-treated patients received focal/grid laser treatment; week 102, 25.2% vs 45.0%. The pegaptanib treatment group showed significantly better results on the National Eye Institute-Visual Functioning Questionnaire than sham for subscales important in this population. Pegaptanib was well tolerated; the frequencies of discontinuations, adverse events, treatment-related adverse events, and serious adverse events were comparable in the pegaptanib and sham groups. The authors
concluded that patients with DME derive clinical benefit from treatment with pegaptanib 0.3 mg and pegaptanib is effective in the treatment of DME and support a positive safety profile.

Wroblewski et al (2009) conducted a dose-ranging, double-blind, phase II trial to assess the safety and efficacy of intravitreous pegaptanib sodium for the treatment of macular edema following central retinal vein occlusion (CRVO). Patients who had CRVO for 6 months or less were randomly assigned (1:1:1) to receive pegaptanib sodium or sham injections every 6 weeks for 24 weeks. At week 30, the primary analysis showed 36% of patients treated with 0.3 mg and 39% treated with 1 mg of pegaptanib gained 15 or more letters from baseline versus 28% of sham-treated subjects. The secondary analysis showed that patients treated with pegaptanib were less likely to lose 15 or more letters compared with sham-treated eyes and showed greater improvement in mean visual acuity. The authors concluded that intravitreous pegaptanib sodium appears to provide visual and anatomical benefits in the treatment of macular edema following CRVO, based on the 30-week study.

The Macugen AMD Study Group (2007) conducted a prospective 2-cohort study with one open-label cohort and one randomized, double-blind, uncontrolled cohort to characterize the safety, tolerability, and pharmacokinetics of pegaptanib in subfoveal choroidal neovascularization secondary to AMD. A total of 147 patients were randomized to receive intravitreous pegaptanib sodium (1 mg or 3 mg) every 6 weeks for 54 weeks. The results showed no IgG or IgM antibodies, few systemic adverse events, and mild or moderate ocular adverse events related to the injection procedure in most patients. Pegaptanib did not accumulate in plasma after multiple doses; systemic exposures were similar after the first, fourth, and eighth doses. Evaluation of blood pressure and urine protein, both of which are known to be affected by systemic VEGF inhibition, indicated no evidence of a pegaptanib treatment effect on these parameters. Mean BP at the end of year 1 remained below 140 mmHg (systolic) and 90 mmHg (diastolic), levels considered hypertension by the American College of Cardiology. The authors concluded that pegaptanib sodium was well tolerated at doses up to 10-fold higher than the 0.3 mg dose approved for treatment of AMD with no detectable clinical evidence of systemic VEGF inhibition and no clinically relevant ocular inflammation.

Gragoudas et al (2004) conducted two concurrent, prospective, randomized, double-blind, dose-ranging, controlled trials to evaluate pegaptanib in the treatment of neovascular AMD. A total of 1186 patients received an intravitreous injection of 0.3, 1.0, or 3.0 mg or pegaptanib or a sham injection every 6 weeks over a period of 48 weeks. Efficacy was demonstrated, without a dose-response relationship, for all 3 doses of pegaptanib. All 3 were significantly different than the sham. In the group given pegaptanib at 0.3 mg, 70% of patients lost fewer than 15 letters of visual acuity compared with 55% among the controls. Significantly more patients receiving pegaptanib (0.3 mg) compared with sham injection maintained their visual acuity or gained acuity. As early as six weeks after beginning therapy with the study drug, and at all subsequent points, the mean visual acuity among patients receiving 0.3 mg of pegaptanib was significantly better than in those receiving sham injections. The authors concluded that pegaptanib appears to be an effective therapy for nAMD.

The VISION clinical trial group (2006) conducted two concurrent, randomized, double-blind, sham-controlled studies to evaluate the efficacy of a second year of pegaptanib
sodium therapy in patients with nAMD. At week 54, patients initially assigned to pegaptanib were re-randomized to continue or discontinue therapy for 48 more weeks. Patients initially assigned to sham were re-randomized to continue sham, discontinue sham, or receive 1 of 3 pegaptanib doses. In combined analysis, mean visual acuity was maintained in patients continuing with 0.3 mg pegaptanib compared with those discontinuing therapy or receiving usual care. In patients who continued pegaptanib, the proportion who lost >15 letters from baseline in the period from week 54 to week 102 was half that of patients who discontinued pegaptanib or remained on usual care. Patients continuing 0.3 mg pegaptanib for a second year were less likely to lose > or =15 letters than those re-randomized to discontinue after 1 year. The proportion of patients gaining vision was higher for those assigned to 2 years of 0.3-mg pegaptanib than receiving usual care. Progression to legal blindness was reduced for patients continuing 0.3-mg pegaptanib for 2 years. The authors concluded that continuing visual benefits were observed in patients who were randomized to receive therapy with pegaptanib in year 2 of the VISION trials when compared with 2 years’ usual care or cessation of therapy at year 1.

Singerman et al (2008) evaluated the safety of up to 3 years of pegaptanib sodium therapy in the treatment of nAMD. At week 54, patients initially assigned to pegaptanib were re-randomized to continue or discontinue therapy for 48 more weeks. Patients initially assigned to sham were re-randomized to continue sham, discontinue sham, or receive 1 of 3 pegaptanib doses. At 102 weeks, patients receiving pegaptanib 0.3 mg or 1 mg in years 1 or 2 continued; those receiving 3 mg or who did not receive treatment in years 1 and 2 were randomized to 0.3 mg or 1 mg for year 3. Pegaptanib was well tolerated in year 3. The authors concluded that the 3-year safety profile of pegaptanib sodium was favorable in patients with nAMD.

**Codes:**

J2503 – Injection, pegaptanib sodium, 0.3 mg

**Medically necessary ICD-10 Diagnosis Codes:**

**References:**

1. Facts and Comparisons 4.0
2. Macugen PI
3. Clinical Pharmacology online


10. VEGF Inhibition Study in Ocular Neovascularization (VISION) Clinical Trial Group, Chakravarthy, U., Adamis, AP., Cunningham, ET Jr., Goldbaum, M., Guyer, DR., Katz, B., Patel, M. Year 2 efficacy results of 2 randomized controlled trials of pegaptanib for neovascular age-related macular degeneration. Ophthalmology. 2006; 113(9):1508e1-25.


Summary of Changes

<table>
<thead>
<tr>
<th>Date</th>
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</thead>
<tbody>
<tr>
<td>1/17</td>
<td>Coding update</td>
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<tr>
<td>5/16</td>
<td>Annual review, no changes recommended</td>
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