Reference number(s)
4461-A

STANDARD MEDICARE PART B MANAGEMENT

MACUGEN (pegaptanib sodium injection)

POLICY

I. 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.

A. FDA-Approved Indication
Macugen is indicated for the treatment of neovascular (wet) age-related macular degeneration.

B. Compendial uses
1. Treatment of diabetic macular edema
2. Treatment of proliferative diabetic retinopathy

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.

II. CRITERIA FOR INITIAL APPROVAL

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

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

C. **Proliferative diabetic retinopathy**
Authorization of 12 months may be granted for the treatment of proliferative diabetic retinopathy.

III. 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:
A. The member is currently receiving therapy with Macugen.
B. Macugen is being used to treat an indication enumerated in Section II.

C. The medication has been effective for treating the diagnosis or condition.

IV. SUMMARY OF EVIDENCE

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

1. The prescribing information for Macugen.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Macugen are covered in addition to the following:

1. Treatment of diabetic macular edema
2. Treatment of proliferative diabetic retinopathy

V. EXPLANATION OF RATIONALE

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

Support for using Macugen to treat diabetic macular edema can be found in a study by Cunningham et al. Administration of intravitreal pegaptanib led to an improvement in visual acuity and a reduction in central retinal thickness in some patients with early-stage diabetic macular edema (DME) in a randomized, double-blind, dose-finding, phase-II trial. Patients (n=172) with visual acuity letter scores between 68 and 25 (Snellen equivalent, 20/50 to 20/320) in the study eye, a minimum score of 35 (20/100 or better) in the other eye, and intraocular pressure no greater than 23 mmHg were eligible. Extensive exclusion criteria were employed, leading to enrollment of patients with early stages of DME. Patients were randomized to pegaptanib 0.3 mg (n=44), 1 mg (n=44), or 3 mg (n=42) or sham (placebo) injection (n=42) administered by intravitreal injection every 6 weeks for a minimum of 3 injections (up to 6 injections). Laser photocoagulation was allowed after week 13 if clinically indicated. Study endpoints included visual acuity (VA), central retinal thickness (CRT) on ocular coherence tomography (OCT) and need for laser photocoagulation. Pegaptanib-treated patients received an average of 5 injections, with 49% (83/172) receiving the maximum of 6 injections. Of the patients receiving the active study regimen, the patients allocated to the 0.3-mg dose had greater improvement in VA, greater decrease in retinal thickness, and lesser need for focal/grid laser intervention. The mean changes in VA (in letters) from baseline to 36 weeks were +4.7, +4.7, and +1.1 for pegaptanib 0.3 mg (significantly different), 1 mg, and 3 mg, respectively, compared to -0.4 in the placebo group. The median VA (in Snellen equivalents) in the 0.3-mg group was better than the placebo group at 36 weeks (20/50 vs 20/63). The mean change in central retinal thickness from baseline to week 36 was significantly better -68 mcm (range, -118.9 to -9.88 mcm) in the pegaptanib 0.3-mg group versus +3.7 mcm in the placebo group. Twenty-five percent (11/44) of the pegaptanib 0.3-mg group and 48% (20/42) of the placebo group received focal photocoagulation between weeks 12 and 36. Common ocular adverse events that occurred more frequently in the pegaptanib groups included: eye pain (31% vs 17%), vitreous floaters (22% vs 7%), punctuate keratitis (18% vs 17%), cataract (13% vs 10%), eye discharge (11% vs 10%), and conjunctival hemorrhage (10% vs 0%).

Support for using Macugen to treat proliferative diabetic retinopathy can be found in small studies that indicate 0.3 mg Macugen once every six weeks by intravenous injection may be effective in slowing disease

progression. The American Diabetes Association recommends that intravitreous anti-vascular endothelial growth factor (anti-VEGF) agents, such as Macugen, may be considered for management of proliferative diabetic retinopathy, especially if high-risk characteristics are present.

VI. REFERENCES

1. Macugen [package insert]. Palm Beach Gardens, FL: Eyetech Inc.; July 2016.
2. IBM Micromedex DRUGDEX [database online]. IBM Micromedex. IBM Watson Health. Accessed January 27, 2023. https://www.micromedexsolutions.com/
3. Clinical Pharmacology [database online]. Elsevier, Inc.; Accessed January 27, 2023. https://www.clinicalkey.com/pharmacology/
4. Cunningham ET, Adamis AP, Altaweel M, et al: A phase II randomized double-masked trial of pegaptanib, an anti-vascular endothelial growth factor aptamer, for diabetic macular edema. Ophthalmology 2005; 112(10):1747-1757.
5. Soloman SD, Chew E, Duh EJ, et al. Diabetic Retinopathy: A position statement by the American Diabetes Association. Diabetes Care. 2017 Mar;40(3):412-418.