The Angiogenesis Foundation

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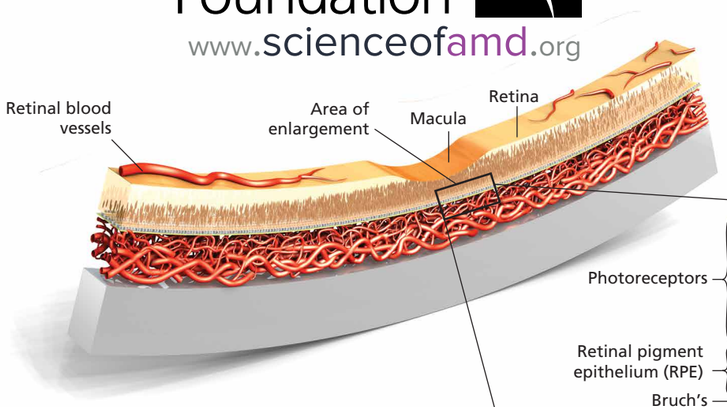
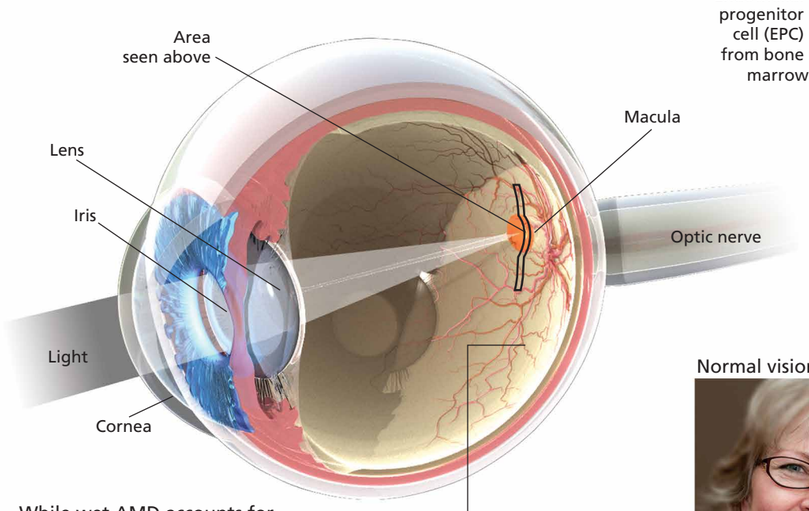
Angiogenesis in Wet AMD

The neovascular form of age-related macular degeneration (wet AMD) is characterized by excessive proliferation of abnormal, leaky blood vessels (angiogenesis) growing from the choroidal layer through Bruch's membrane and into the retinal layers. If left untreated, the proliferating vessels will eventually cause a subretinal fibrotic scar and permanent vision loss.





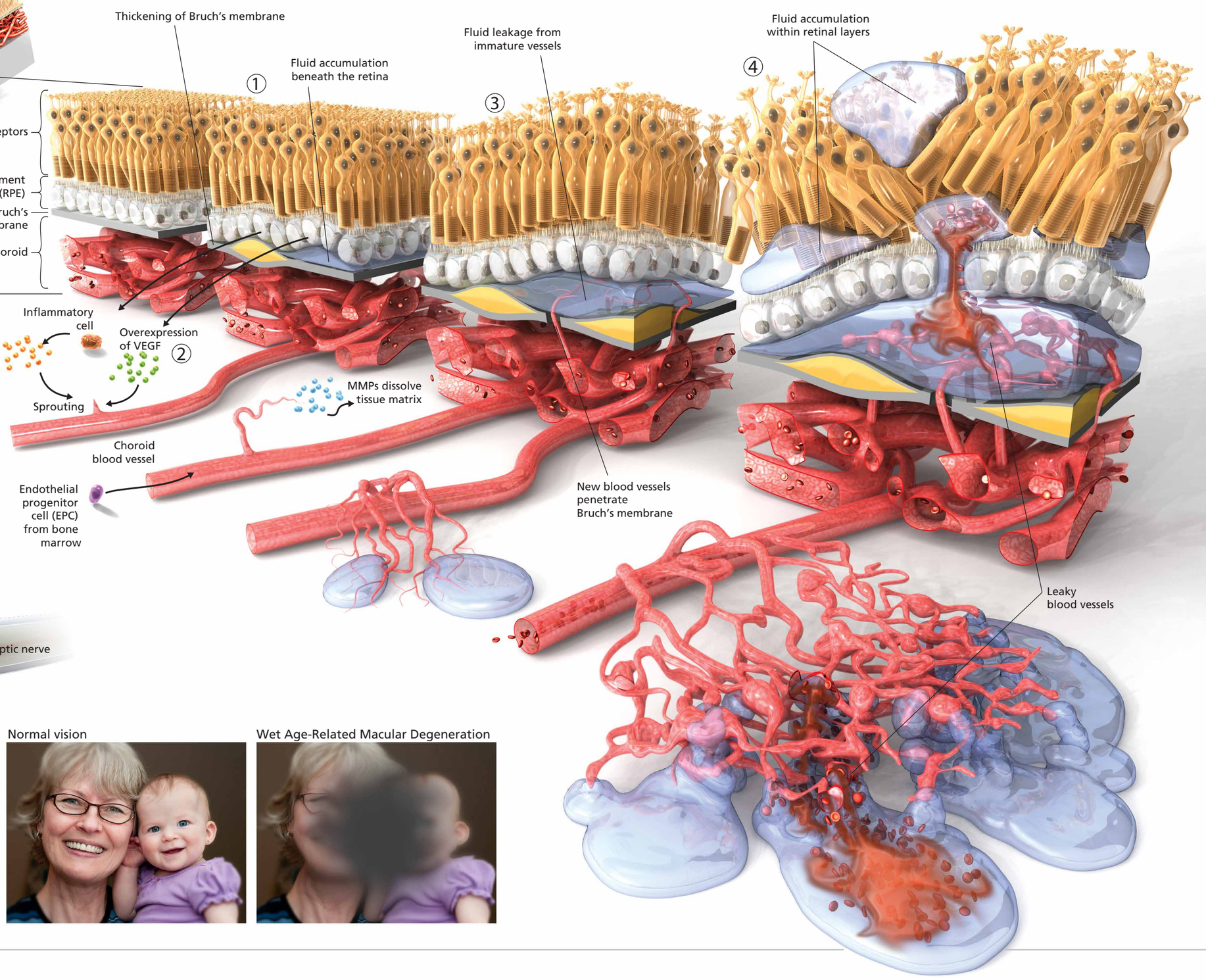
While wet AMD accounts for only about 10-15% of all AMD cases, this form is responsible for up to 90% of severe vision loss or legal blindness from the disease.

① Oxidative stress such as UV light exposure, aging, and smoking, as well as genetic predisposition, leads to inflammation in blood vessels. With age, Bruch's membrane can thicken, causing hypoxia in the retina and RPE.

② In response to inflammation, inflammatory cells are recruited to the retina. These recruited cells, as well as the RPE, secrete angiogenic growth factors such as VEGF and inflammatory cytokines.

③ The growth factors stimulate the growth of blood vessels in the choroid layer. These vessels then penetrate the Bruch's membrane, and fluid begins to accumulate within and below the retinal layer.

④ The new blood vessels are disorganized and leaky. The leaked fluid lifts the retina away from the RPE and Bruch's membrane.

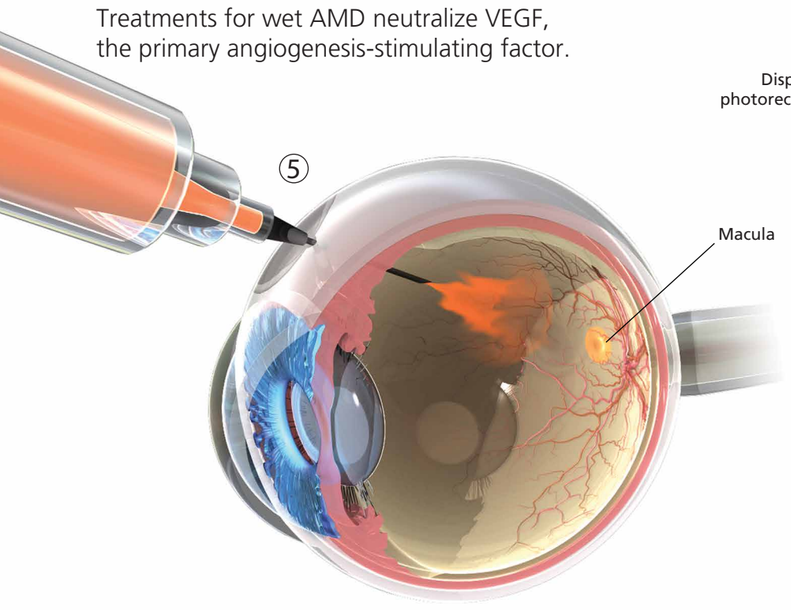


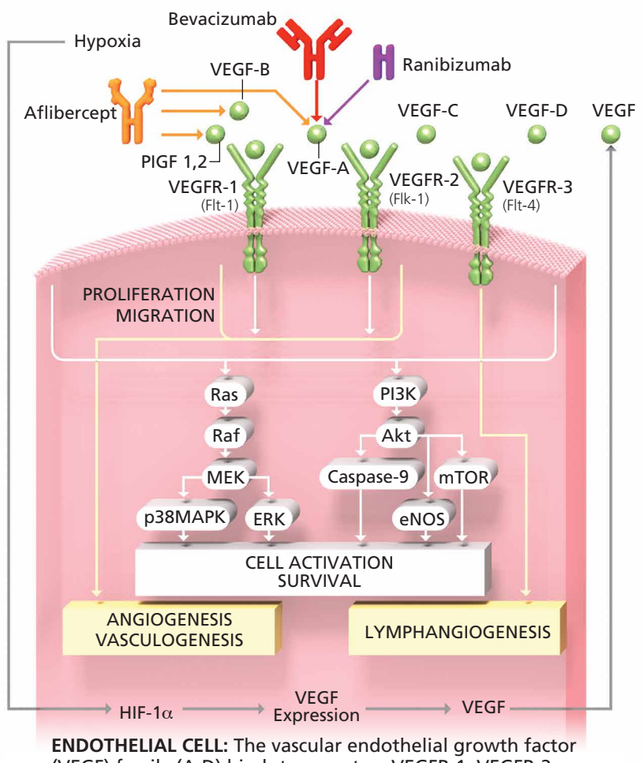
Normal vision

Wet Age-Related Macular Degeneration

Antiangiogenic Treatments

Treatments for wet AMD neutralize VEGF, the primary angiogenesis-stimulating factor.



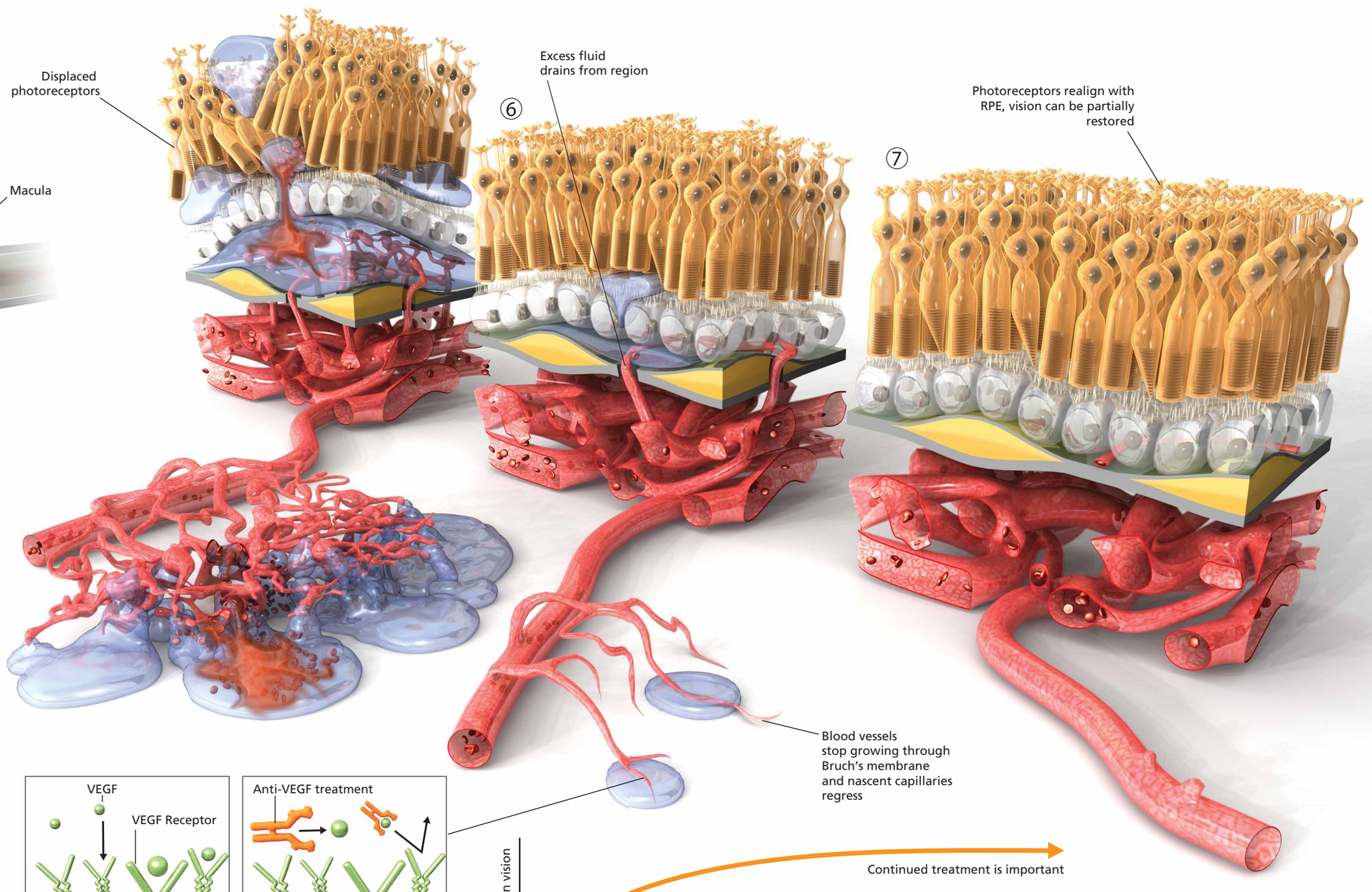


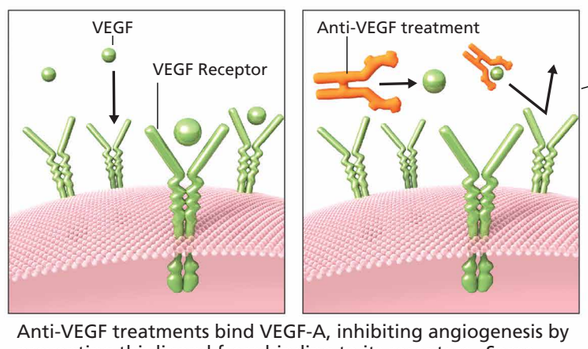
ENDOTHELIAL CELL: The vascular endothelial growth factor (VEGF) family (A-D) binds to receptors VEGFR-1, VEGFR-2, VEGFR-3, activating signal transduction to promote angiogenesis, vasculogenesis, and lymphangiogenesis.

⑤ The three major anti-VEGF therapies, Ranibizumab, Bevacizumab, and Aflibercept, are administered intravitreally (injected directly into the eye), usually at monthly or less frequent intervals.

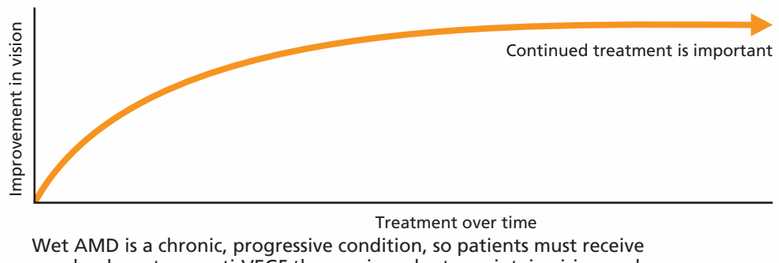
⑥ Inhibiting excessive VEGF in the eye causes regression and maturation of abnormal, leaky capillaries, and reduces fluid accumulation. Many patients experience an improvement in vision very soon after treatment.

⑦ With prolonged VEGF blockade, the accumulation of fluid beneath the retina resolves and the photoreceptors reattach to the underlying retinal pigment epithelium.





Anti-VEGF treatments bind VEGF-A, inhibiting angiogenesis by preventing this ligand from binding to its receptors. Some therapies can specifically bind to related ligands, such as VEGF-B and PlGF.



Wet AMD is a chronic, progressive condition, so patients must receive regular, long-term anti-VEGF therapy in order to maintain vision and slow the advance of the disease.

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